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The Antiseptic

A Monthly Journal of Medicine & Surgery

Founded by the late Dr. U. RAMA RAU in 1904. Published on the 15th of every month

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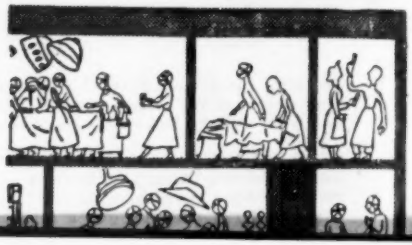

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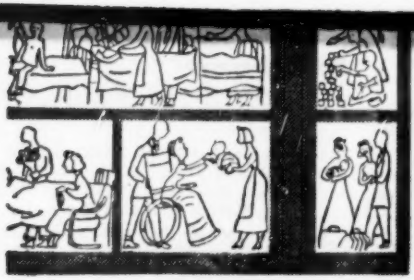

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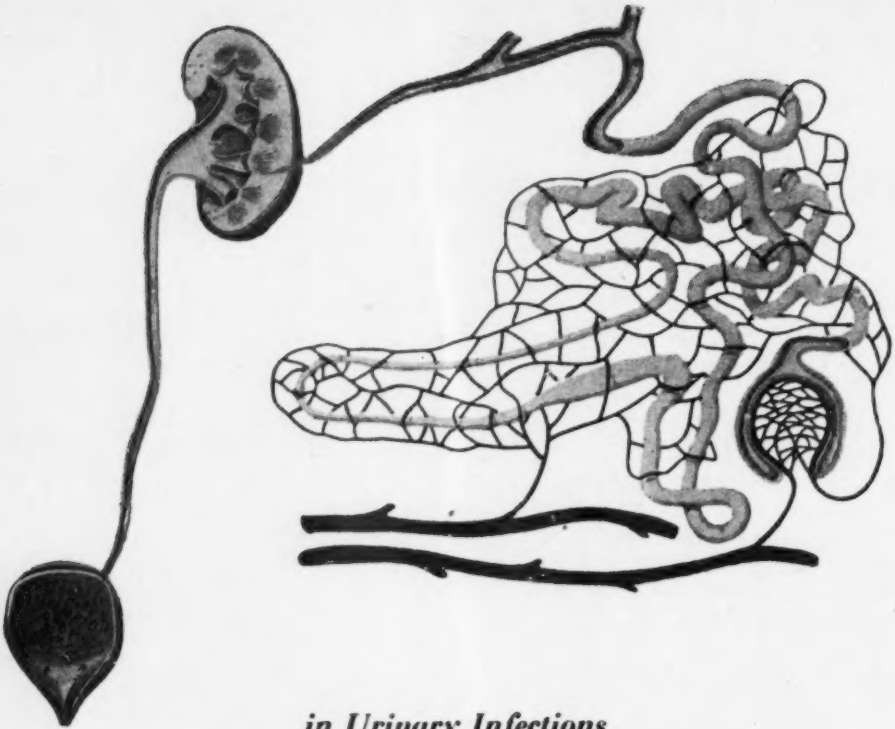

in Urinary Infections

SULFADIAZINE

Sulfadiazine remains a sulfonamide of choice in the initial therapy of many acute uncomplicated cases of genitourinary infection. It has been found effective against gonorrhea, with relatively little danger of producing an appreciable increase in the resistance of the organism. In chronic resistant urinary infection, particularly in the presence of obstructive lesions, it will usually be found necessary to associate with sulfadiazine some antibiotic such as aureomycin. While control of the infection may thus be obtained, it is essential for permanent cure that a free flow of urine be assured. In many cases, surgery for the relief of obstruction will prove to be necessary.

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Original Articles

CORTICOTROPHIN IN STATUS ASTHMATICUS AND HOMOLOGOUS SERUM HEPATITIS *

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Introduction.—Ever since corticotrophin and cortisone became generally available, a diverse group of apparently unrelated diseases have been treated with these agents with varying success. Extensive literature has been published on the use of these hormones and their hazards in foreign medical journals. Reports on their use in our country have not, however, been so far published. This report describes the effect of corticotrophin in two entirely unrelated diseases—*viz.*, status asthmaticus and homologous serum hepatitis.

CASE 1.—A female patient, Mrs. J. S., aged 65 years, was admitted in Sheth Vadilal Sarabhai General Hospital on 21-12-'52 with the following complaints :—(1) Extreme breathlessness and (2) cough with expectoration of 8 days' duration. She was having such attacks of breathlessness for the last 16 years.

Nothing significant was found in the personal history of the patient and no other previous illness of importance. There was no family history of asthma.

* Specially contributed to THE ANTISEPTIC.

Examination on admission.—The patient was in an orthopnœic position, with extreme breathlessness, cyanosis of the lips and nails and the accessory respiratory muscles were in action. The temperature was 98°F., pulse 120 p.m., resp. 34 p.m. The patient was markedly anæmic with flattening of the nails. No puffiness of the face, nor œdema of the legs, or free fluid in the abdomen was detected. Examination of the cardiovascular, gastro-intestinal, nervous and genito-urinary systems revealed no abnormality.

Examination of the respiratory system showed diminished respiratory excursions, with the chest fixed in a position of inspiration, a hyper-resonant note on percussion all over the chest, and prolonged expiration with wheezing rhonchi and scattered rales on both sides of the chest.

Laboratory Investigations

21–12–'52 :—Blood examination : Total W.B.C. 15,100. Differential count :—P. 82 per cent ; L. 15 per cent ; Eos. 2 per cent ; Mono. 1 per cent.

27–12–'52 :—Blood examination : Total W.B.C. 11,800. Differential count :—P. 92 per cent ; L. 7 per cent ; Mono. 1 per cent.

3–1–'53 :—Blood examination : Total W.B.C. 18,400. Differential count :—P. 95 per cent ; L. 5 per cent ; Eos. nil ; Mono. nil ; Total R.B.C. 4,080,000 per cmm. Hb. 48 per cent ; C.I. 0·6.

Blood potassium :—18 mg. per 100 c.c.

OTHER INVESTIGATIONS : —*Screening of chest* :—No abnormality seen in the lungs or heart.

Electrocardiogram :—No pathology in the heart.

TREATMENT :—The patient was treated with 0·5 gm. of aminophylline and 100 mg. of viscardan twice a day for three days. Response to treatment was however, not very satisfactory. Oxygen was administered by a nasal catheter. Patient did not show any evidence of Co_2 narcosis, as reported by Schiller and Lowell (1951).

The patient was switched on to ACTH on 24–12–'52 and the following dosage schedule was adopted :—

25 mg. ACTH I.M. every six hours *i.e.*, 100 mg. per day for four days, from 24–12–'52 to 27–12–'52. 20 mg. of ACTH I.M. six hourly *i.e.*, 80 mg. per day for two days from 28–12–'52 to 29–12–'52. 12·5 mg. of ACTH I.M. six hourly *i.e.*, 50 mg. per day for two days from 30–12–'52 to 31–12–'52. 10 mg. of ACTH six hourly *i.e.*, 40 mg. per day for two days from 1–1–'53 to 2–1–'53. 5 mg. of ACTH six hourly 20 mg. per day from 3–1–'53 to 4–1–'53, the total dose of ACTH given in eleven days being 760 mg.

During ACTH treatment, the weight of the patient, his blood pressure and the urinary output in twenty four hours, were,

recorded. The urine was examined for sugar everyday. Following are the figures :—

Date	Weight	B.P.	Quantity of urine	Sugar
24–12–'52	97 lbs.	120/60	25 ozs.	Nil
25–12–'52	Do.	134/54	28 ,,	,,
26–12–'52	Do.	144/64	30 ,,	,,
27–12–'52	Do.	160/60	37 ,,	,,
28–12–'52	Do.	154/60	20 ,,	,,
29–12–'52	Do.	160/60	58 ,,	,,
30–12–'52	Do.	140/60	26 ,,	,,
31–12–'52	Do.	120/50	47 ,,	,,
1–1 —'53	99 lbs.	140/40	39 ,,	,,
2–1—'53	100 lbs.	130/60	29 ,,	,,
3–1—'53	100 lbs.	128/60	28 ,,	,,

On the 28th December a mercurial diuretic was given because of oliguria and the response was satisfactory ; the patient during treatment was on milk diet, hence the question of salt and fluid restriction did not arise. Prophylactic penicillin, 10 lacs per day and 4 gm. of potassium were administered throughout the course of treatment. Plastules with folic acid were given for the anæmia.

Results of treatment, discussion and comment.—After the fourth day of administration of ACTH, dyspnœa and cyanosis completely disappeared and the patient was able to sleep in bed comfortably in the lying posture. Wheezing sounds in the lungs though diminished in intensity, had not completely disappeared. A good remission in an otherwise intractable condition had thus been obtained. It remains to be seen how long this remission will be maintained. The patient developed puffiness of the eyelids and a gradual gain in weight of 3 lbs. in 11 days. For the first 8 days the weight remained constant, puffiness of the eyelids was still present. Oedema was thus due to movement of fluid from the cells into the extra-cellular tissue-spaces, and not due to retention of ingested fluid, because the weight remained unaltered. This phenomenon has been observed by Lippett in experimental animals. Using inulin as a measure of extra-cellular fluid space, he showed that a shift of fluid from cells into the extra-cellular tissue spaces occurred when ACTH was administered to experimental animals, on a salt-free diet with rigid fluid restriction. This shift of fluid occurred up to the 8th or 9th day of therapy—after which the normal fluid balance between the cells and the tissue spaces was again restored—irrespective of whether treatment with the hormonal agent was continued or not. This experimental observation of Lippett was confirmed clinically in my patient. Speaking before the scientific meeting of the Second International Congress of Internal Medicine—held in London on 16th September 1952—Prunty stated that "in ACTH therapy œdema could arise without obvious fluid-retention, suggesting that there was transference of fluid from the cells to the extra-cellular tissue-spaces. Further studies on this problem are in progress.

Blood pressure was elevated during treatment, especially the systolic pressure, the maximum systolic pressure recorded after 6 days was 160 mm. of Hg.; the diastolic pressure was not however, altered. No other metabolic deviations were observed.

As was to be expected, the total W.B.C. count rose from 15100 to 18400 per cmm. This was due to an absolute increase in the number of neutrophile leucocytes, because lymphocytes fell from 15% to 5% and the eosinophils from 2% to 0% during therapy.

Taking into consideration the fact that the patient was in an extremely critical condition at the commencement of the treatment, the result achieved should be considered truly remarkable.

Summary and conclusions.—(1) A case of status asthmaticus treated with ACTH is reported. (2) The effect on fluid-balance between the cells and the tissue-spaces and on the blood-pressure is discussed. (3) ACTH is found to be a life-saving remedy in this condition when all the other conventional methods of treatment have failed.

CASE II.—A female patient, Mrs. J. K.,* aged 35 years, was admitted under my care at the Sheth Vadilal Sarabhai General Hospital on 5-1-'53 with the following complaints:—

(1) Jaundice of three months' duration. (2) Nausea and vomiting in the morning. (3) Fever with rigors up to 99°F to 100°F for the previous 10 days. (4) Discomfort in the chest and epigastrium and pain in the abdomen around the umbilicus. (5) Headache—and a burning sensation on the top of the head.

Six and a half months ago the patient had an abortion, at two and a half months' pregnancy. After this incident she had profuse and irregular bleeding for a month and a half, which produced a moderate anæmia. She had therefore, received a blood-transfusion of 200 c.c. about 5 months ago. Her anæmia then gradually improved and her menorrhagia was also controlled. Two months later, the patient had fever for a week and developed an yellowish tinge in the conjunctiva. The fever subsided but the concomitant symptoms of jaundice, loss of appetite, nausea, vomiting, pain in the right hypochondrium, yellowish discolouration of the skin, and generalised itching, developed. Ten days prior to admission in the hospital, the patient again got fever up to 99°F to 100°F, which persisted for two days while in hospital. No other member in her family had suffered from jaundice.

Examination on admission:—Skin and conjunctiva showed an yellowish tinge. Nails were pale. Pulse, 96 p.m. Resp. 24 p.m., B.P. 110/70 mm. Hg. Gastro-intestinal system:—abdomen was soft and flabby; spleen enlarged 3 fingers below the costal margin;

* This patient was seen again on 12-2-1953: Jaundice had cleared up completely though vague symptoms of neurosis remained.

liver enlarged two fingers below the costal margin and tender on pressure. Examination of the circulatory, respiratory and genito-urinary system, and gynæcological examination revealed no abnormality.

Laboratory investigations:—R.B.Cs. 4·2 million per cmm. W.B.C. 5,600 per cmm. Hæmoglobin 86%. Differential count: P. 77%; L. 17%; E. 6%

Vanden Berg reaction:—Direct immediate positive (6-1-'53). Direct immediate faintly positive (13-1-'53):—Icterus index 12 (6-1-'53); 8 (13-1-'53).

Plasma proteins: Total proteins 6·15 gm. per 100 c.c. Albumin: 4·73 gm. per 100 c.c. Globulin: 1·42 gm. per 100 c.c. Takata Ara test: negative. Fasting blood sugar: 102 mg. per cent. Blood potassium: 16·6 mgm. per cent. *Urine examination*: Albumin absent, sugar absent, bile salt present. Bile pigments present, microscopically no abnormality seen. *Stools examination*: Reaction alkaline; small mucus flakes with epithelial cells 20 to 50, pus cells 50 to 100 macrophage 10 to 30, and R.B.Cs 5 to 15 per high power field. *Gastric analysis*: Total acidity 70 and free acidity 60—after two and a half hours. *Other investigations*: (1) Screening of chest: Heart and lungs normal. (2) Barium meal screening of stomach and duodenum: Stomach low, hypotonic. Duodenal cap normal. (3) X-ray for gall stones: No gall stone seen in plain X-ray picture.

On the basis of the history, physical findings and the laboratory investigations, the diagnosis of homologous serum jaundice was made.

Prior to hospital admission, the patient had been treated along conventional lines. Response to treatment was, however, unsatisfactory and relapse occurred 10 days prior to admission in the hospital. It was, therefore, decided to treat the patient with ACTH. The patient was put on a salt-free diet with moderate fluid restriction. The weight of the patient, blood pressure and twenty-four hours' urinary output were recorded every day. Urine was examined every day during therapy for sugar and ketone bodies.

The following dosage schedule was used:—12·5 mg., six hourly intramuscularly—every day for 11 days. Total amount of ACTH given in eleven days was 500 mg.

Adverse effects:—On the fourth day of treatment nervousness was exaggerated, and the patient complained of discomfort in the chest and epigastric pain, hence fearing the precipitation of psychotic disturbance, the hormone was stopped for 18 hours *i.e.* 3 doses were omitted. It was restarted after this period—the dosage used for the next 24 hours being 5 mg.—six hourly. From the next day 12·5 mg. six hourly was again given. On the 8th day of therapy the patient again complained of epigastric pain, which became worse after food. Gastric analysis done on the ninth day showed increased total and

free acidity ! Barium meal screening of the stomach and duodenum was also done. No evidence of gastric ulcer was detected. Treatment was, therefore, continued till the 12th day. The patient also complained of sourness of the mouth after the 8th day of treatment.

Highest blood pressure recorded on the 5th day was 134 mm. systolic and 90 mm. diastolic. There was no appreciable gain in weight nor conspicuous œdema. Urine examination showed neither sugar nor ketone bodies throughout the course of treatment. The output of urine varied between 15 ozs. and 60 ozs. No other metabolic deviations were detected.

In addition to ACTH :—(1) Potassium 4 gm ; (2) Injections of penicillin 5,00,000 units and streptomycin 0·5 gm. twice a day ; (3) methyl testosterone tablets ; (4) aluminum hydroxide ; (5) and Siledin tablets, were given as and when required. Methionine, choline and protein hydrolysate were also given throughout the course of treasment.

Results of treatment, discussion and comment.—Within a week of the administration of ACTH the patient experienced a sense of mental well-being and the appetite which had been completely lost also gradually returned. At the end of the therapy the patient's appetite had considerably improved and nausea, vomiting, abdominal discomfort had all disappeared. Subsequently, the sense of burning on the top of the head and discomfort in the chest however, persisted. Pruritus also ceased. Objectively the liver was no longer palpable nor tender, icteric tinge in the skin and the conjunctiva became less marked, and the icterus index fell from 12 to 8.

Liver biopsy, which would have given precise data regarding the regression of the inflammatory process, was not done.

Warthin and Dalrymple reported good results with ACTH and cortisone in acute viral hepatitis, and less successful ones in patients with chronic active hepatitis. They concluded that "all patients had marked subjective improvement, diminution of liver size, reduction of jaundice and clearing of inflammation on biopsy. Relapses were, however, common. ACTH and cortisone have then some hope of improving the course of chronic liver disease, when acute inflammation is present. They also produce a sense of well-being, and improved appetite, so that a diet of high caloric value can be given".

Colbert *et al* (1950) also reported similar results. They treated five cases at the 98th General Hospital, Munich, with ACTH and found a prompt return of the appetite and disappearance of jaundice and pruritus. In their cases there was no definite change in liver tenderness, and the serum bilirubin level fell and rose again after cessation of the therapy. Cephalin cholesterol flocculation and thymol turbidity tests did not follow such a clear trend, although

they tended to return to normal. ACTH sensitisation was observed in one patient.

The case here reported confirms the results obtained by the above investigators.

Summary.—(1) A case of homologous serum hepatitis treated with ACTH is described.

(2) The literature on the subject is reviewed.

(3) ACTH is found to produce improvement in this condition.

Acknowledgment.—My thanks are due to Dr. M. D. Desai, M.S., F.R.C.S., M.Ch., Orth., Superintendent, Sheth Vadilal Sarabhai General Hospital and Sheth Chinai Maternity Home, for allowing me to publish these cases and to my house-physician Dr. Miss J. H. Gandhi, M.B., B.S., for preparing the notes of the cases. I am grateful to Mr. N.P. Desai for preparing the manuscript.

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Vitamin B_{12} in the Treatment of Asthma

In a note dealing with the treatment of asthma Rouques (*Presse Medicale* 60, 1625) discusses the results obtained by Caruselli (*La. Rif. Med.*, 66, 840) by subcutaneous injections of Vit. B_{12} in twelve adult patients suffering from asthma.

They received a daily subcutaneous injection of 30 microgrammes of vitamin B_{12} for fifteen to twenty days. In only two of the twelve patients, satisfactory results were not obtained. These two were old people of sixty one and sixtyfive years respectively who had a long history of catarrh and asthma and had developed pulmonary emphysema with arteriosclerosis and hypertension.

In the other ten cases the asthmatic crises decreased and later disappeared. In two of these 10 cases, there was a recurrence at the end of three months and eight months respectively, which however, responded rapidly to resumed treatment with vitamin B_{12}. The patient's general condition improved, there was gain in weight, an increase in the erythrocyte count, and a feeling of general well-being. The vitamin B_{12} appeared to act more rapidly in those cases in which there was no inflammatory factor.—(*The Practitioner*, p. 316, March 1953).

SCIATICA DUE TO INTERVERTEBRAL DISC INJURY*

INDRANATH SOBTI, B SC., M.S., F.C P.S.
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THERE are few painful conditions so perplexing and so very trying as sciatica. When we come across a large number of patients suffering from this trouble we are astonished to find the versatile picture of their suffering. For some it is just an irritating malady which does not seriously come in the way of their regular avocation except during an occasional attack of more severe pain, while it keeps others almost completely bedridden and miserable. This is not in any way surprising in view of the fact that this symptom complex is due to a variety of pathological conditions, not only in the lumbosacral region but in the body as a whole. In the lumbosacral region, muscle strain, ligamentous injury, subluxations, arthritis, intervertebral disc injury etc. may be some of the causes of sciatica. The whole problem becomes very complex as in this region the various muscles, fascia, ligaments and joints are all supplied by the same group of nerve fibres and pain arising in any of these may be referred to the back of the thigh. Besides this neuralgic type of sciatica, there are conditions in which there is actual inflmmation, compression, or irritation of the sciatic nerve or its roots in any part of its course. All these different conditions can produce sciatic pain and it is no wonder that a simple treatment which relieves one patient may prove absolutely worthless for another. One of these conditions which is satisfactorily treated by operation is the intervertebral disc injury with herniation of the nucleus pulposus. The aim of this operation is to relieve pressure on the affected nerve root. Of the many causes that can injure the intervertebral disc the most important seems to be compression or flexion of the spine. Manipulation of the spine under anæsthesia and injury by the lumbar puncture needle can also cause herniation of the nucleus pulposus. Degenerative changes in the annulus fibrosus may cause it but a little trauma is the exciting cause. The herniation is usually between the fourth and fifth lumbar vertebræ or between the last lumbar vertebra and the first sacral vertebra. Usually it is asymmetrical and on one side. Rarely a big protrusion may be centrally placed and press the roots on both sides.

Report of a case.—An adult male D., aged 41 years came to the out-patient department of Seth J. P. Bhartia Hospital, Fatehpur Rajasthan on 26-4-'51 with a complaint of pain in the region of the distribution of the left sciatic nerve since 7 years. He was given salicylate with iodide and aspirin. He came again 5 days later when he was referred to me. He had practically no relief

* Specially contributed to THE ANTISEPTIC.

Sciatica due to Intervertebral Disc Injury
Indranath Sobti.

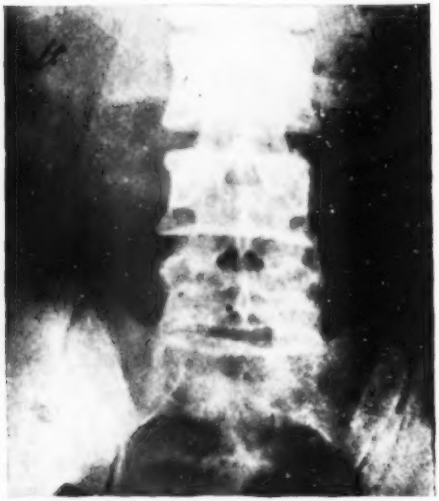

FIG. 1 [*Vide page 553.*

FIG. 2

The 4th and 5th L. spines have been excised, and a window made after excising lower margin of the lamina of 5th L. vertebra and ligamenta flava. S. 1. root is seen on the left side. On retraction of this root medially, the small white knob is seen. [*Vide page 554.*

and I advised epidural saline injections. Even this gave very little relief and he was therefore, admitted as an in-patient on 3-5-'51.

HISTORY :—About 10 years ago the patient developed sudden pain in his lumbar region while lifting a heavy weight. The pain was very severe and persisted for a few days, and then gradually disappeared. After 3 years he got another attack of pain while lifting some object but this time the pain got gradually shifted from the lumbar region to the region of the distribution of the sciatic nerve on the left side. The pain gradually decreased in intensity and passed off in about a month's time. Thereafter he remained almost free from any pain for nearly 6 years. Now again since the last 6 months *i.e.*, nine and a half years after the first attack of pain in the lumbar region he is getting pain in the left sciatic distribution. The pain is persisting and gets more severe in the early mornings, and also increases when the patient walks or even stands.

Examination :—There was no deformity in the lumbar spine. The left inferior extremity was slightly wasted and the gluteal muscles on the left side were weak and flabby. The movements of the lumbar spine were limited to some extent in all directions. There were no sensory or motor disturbances in the inferior extremities. The knee and the ankle jerks were normal on both the sides. *Straight leg-raising-test*—Pain was felt in the region of the left sciatic distribution as soon as the leg was raised to 30°. *Naffziger's test*—Compression of the jugular veins in the neck in the standing position produced tingling and numbness in the postero-lateral aspect of the left leg. *Lumbar puncture*—The cerebrospinal fluid was normal in appearance. X-ray of the lumbar region was normal. (*Vide Fig. 1*).

TREATMENT :—He was confined to the bed and salicylates, iodides, vitamin B etc. were continued. Epidural saline was given on more than 3 occasions and 10 diathermy sittings of 10 minutes' duration, each were given. All these gave very little relief and the moment he tried to get up severe pain started in the sciatic region. The patient got fed up and felt very miserable. Plaster jacket was considered but given up as the patient was unwilling, due to the sweltering heat. It was therefore, decided to operate upon him.

Anaesthesia :—Spinal was supplemented with general anæsthesia at the end of the operation.

Operation (19-6-51) :—He was placed in the right lateral position and the skin of the lumbo-sacral region which was shaved and prepared a day earlier, was repainted with tincture of iodine. A midline incision about 6 inches long was made extending from the second lumbar spine to the third sacral. The sacrospinal muscles were separated from the spinous processes and the laminæ with an osteotome. Hot packs were used to stop oozing. Having cleared the laminæ the spinous processes and the ligaments between the

laminæ, the 4th and 5th spinous processes were excised. The lower margin of the lamina of the 5th lumbar vertebra was removed and the ligamenta flava in this window was excised. Some extra-dural fat was then removed with an ordinary pair of forceps exposing the nerve roots (S. I.) (*Vide Fig. 2*). The extra dural fat was further removed and the nerve root on the left side was gently retracted medially. This exposed a small white knob about 3 mm. x 3 mm. lying in front of the nerve root. This knob was incised and its contents removed with the help of a fine crocodile forceps and a fine ear forceps. The contents consisted of shreds of whitish tissue. The white knob was much smaller than was expected and a doubt arose as to whether it could be the sole cause of the trouble. It was therefore, decided to expose the 5th lumbar root also. The lower margin of the fourth lamina and the remaining part of the fifth lamina on the left side were excised and the extra dural fat cleared. Here the root was normal and no white knob was discovered. The wound was then dusted with penicillin powder and closed in three layers (muscles, aponeurosis, and skin) as usual after keeping a small drain at one end of the wound.

POST-OPERATIVE TREATMENT:—He was transferred to a hard surfaced bed and kept in the lateral position for some time. There was some oozing and he was given morphine, vitamin K and Coagulen (Ciba) thrice in 24 hours. He was also given sulphadiazine and penicillin prophylactically. The drainage tube was removed after 48 hours. The stitches were removed after 10 days. He complained of pain in the lumbar region for a few days, and was therefore, kept in bed for some more days. He was discharged on 29-7-'51. At the time of his discharge he had no pain anywhere but he walked very cautiously lest the pain might return. He came to the hospital on 28-8-'51, a little over 2 months after his operation. He said that he got some aching sensation in his buttocks after prolonged sitting but the sciatic pain had completely disappeared. He was very much satisfied and thankful. He was told to resume his occupation (tailor) and reassured that the buttock pain would gradually disappear.

Summary.—A case is described of severe sciatica that resisted all conservative methods of treatment. He was then operated and the contents of the prolapsed disc evacuated extradurally, with complete relief.

Surgical Treatment of Sciatica

The operation involves hemilaminectomy, removal of the protrusion, and curetting out nuclear material from the central part of the disc. The patient should be in bed for 3 weeks and convalesce for some time before resuming work. For residual symptoms which may persist, radiant heat and massage or diathermy are often used; the *constant current* is helpful symptomatically. —(*Practitioner*, Feb. 1953, p. 198).

PROTEINS IN NUTRITION*

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Introduction.—Our bodies which look so solid and substantial and real are only so in appearance; 78 per cent of them consist of the gases oxygen, hydrogen and nitrogen ([9]). These we derive from our food. The substances which supply nitrogen are called nitrogenous compounds. The older workers designated them as albumins or quaternary azotized compounds, but to-day we call them proteins.

The word "protein" was first used by the Dutch Chemist Mulder in 1838 ([1]). The word protein was derived from the Greek "Proteios" meaning "of the first rank or position". Of the three proximate principles of our food *viz.*, carbohydrates, fats and proteins, the latter are the most important because of the multiplicity of their biologic functions.

Protein is the essential constituent of all living cells, without which life cannot exist. The need for protein in the diet was first pointed out by Francois Magendie (1816), the great French physiologist, who attempted to see whether animals could live without nitrogenous food.. Dogs kept on sugar or fat and distilled water became emaciated and died. Magendie concluded that animals cannot live without nitrogenous food ([37]). Most of the tissues of the body are made up largely of protein. No other substance can take its place. The human body consists of about 18 per cent of protein ([28]).

Proteins are needed to supply material for building body tissues and for the construction of many hormones and enzymes. Pepsin, trypsin and other enzymes necessary for digestion are protein in nature. Insulin and thyroxine are also part proteins.

To realise how diverse are the functions of protein, one has only to think of the proteins of hair and skin, cartilage and blood, of muscles and nerves, and of other intra-cellular and extra-cellular fluids. Nucleoproteins are intimately involved in the processes of cell division, and therefore, reproduction and heredity. Widely different substances such as silk, wool and even leather owe their characteristics to specific proteins.

Protein rarely occurs in a pure or free state. The only example of a food protein one can think of is egg-white. No such example can be given from the vegetable kingdom.

All proteins are made up principally of carbon, hydrogen, oxygen, and nitrogen. Most proteins also contain small amounts of sulphur or phosphorus. But it is the nitrogen, as we have already stated in the beginning, that is the distinguishing characteristic of protein. The number of identified proteins is extremely large and is

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growing rapidly ; according to one observer, (Mathews 1939), the number of tissue proteins in man is estimated to be 1600 ([34]).

How much protein do we need ?:—How much protein do we need ? As protein is the chief material for tissue-building, the body depends upon it for growth, maintenance, repair, reproduction and lactation. The protein requirements accordingly vary in infancy, adulthood, convalescence, pregnancy and lactation. Let us first consider the protein requirements of an adult.

The adult is not called upon to build any new tissue but he needs protein to replace the wear and tear on his tissues due to life processes. In scientific parlance, he has to maintain himself in nitrogen equilibrium.

After experiments on dogs and dietary surveys of men *Carl Voit* was convinced that 118 gm. of protein daily was the desirable standard. This level known as the Voit standard was set forth in 1881, and accepted by many scientists of the day. Voit was supported by his American student Atwater. The latter published in 1894 dietary surveys of industrial workers in New England which showed that it was common practice to consume 118 gm. or even more of protein per day ([5]).

But the Voit standard had many opponents. Hirschfeld was the first outstanding physiological chemist to demonstrate that 40 to 45 gm. of protein daily is adequate to maintain equilibrium in men. Siven a Finn, demonstrated that his body could maintain nitrogen equilibrium on 28 gm. of protein daily, if he consumed with it an adequate quantity of non-protein calories. In 1904, Chittenden who was performing experiments on human beings at the Yale University, showed that about a third or half of the Voit standard was sufficient for health, fitness and nitrogen equilibrium. He suggested that a protein intake of 44 to 53 gm. fully meets the physiological needs of the body of a 70 kg. man. This low protein diet in his opinion "holds out the promise of greater physiological strength, increased endurance, greater freedom from fatigue and a condition of well-being that is full of suggestion for the benefit of health ". In his own case, rheumatism of the knee joint disappeared, and bilious attacks no longer occurred periodically as before ([21]).

Striek (1937) reported on two cases who lived vigorous happy lives on a remarkably low intake of protein. One lived on 38 to 40 gm. of protein for fifteen years, and climbed mountains at the age of 70 ! Another ate about 30 to 40 gm. of protein for 25 months and during this period climbed 22 mountain peaks ! ([38]).

On the other hand, Stefanson lived for long periods in the Arctic circle, exclusively on meat, and experienced the highest degree of physical and mental well-being. The daily diet of the Greenland Eskimo contains 280 gm. of animal protein. Newburgh and his associates (1930) kept a healthy man aged 33 for six months

on a diet containing 337 gm. of protein without ill-effects. Another report described an experiment on two healthy young men who lived for a year upon an exclusive meat diet and felt quite fit. The blood-pressure of one of them fell 20 mm. and that of the other remained normal. Their renal function tests were normal (38). But these are extreme cases. The modern tendency is to strike a middle path. It is argued, "even though sufficient to keep an individual in nitrogen equilibrium, a low protein intake cannot be considered optimal, or even safe for any length of time, for it does not furnish any elasticity for increased demands in the case of intercurrent illness or for small inadvertent changes in the diet. Further, other nutrients such as certain minerals and vitamins of the B complex group which are found associated with protein foods may also be consumed in amounts below the optimum" (49). Therefore, Sherman and others of his school suggest a daily allowance of 1 gm. of protein per kg. of body weight" to provide a margin of safety, from 50 to 100 per cent". This standard has been accepted almost universally and the Food and Nutrition Board of the National Research Council of America has also adopted it. The recommended allowances are, 70 gm. for a man weighing 70 kg. and 60 gm. for a woman weighing 56 kg. (36).

We would naturally like to know if this standard also applies to Indian conditions. The Indian nutrition experts recommend 82 gm. for an adult man and 67 gm. for a woman (27). In view of the fact that the protein requirements vary according to the size of the body and the average Indian is lighter, the above allowance is in my opinion unnecessarily high, because it works out to about 1·5 gm. per kg. of body weight.

(The Indian experts have given the average weights as 55 kg. for man and 45 kg. for woman). Basu and others determined the minimum protein requirement of Indians living on typical Indian dietaries and found it to be 46·4 gm per 70 kg. of body weight. Allowing a 50% margin of safety, the optimum works out to 69·6 gm. or 1 gm. per kg. of body weight (4), which is the same as the Sherman standard. On this basis an average Indian weighing 55 kg. would require 55 gm. of protein and not 82 gm. as the Health Bulletin recommends. But as Lewis has pointed out in his introduction to *Proteins and amino-acids in nutrition*, "This is definitely the era of higher dietary protein" and "dietary protein in amounts far above those of Sherman's recommendations has been advised even for patients seriously ill" (32).

In support of this view may be cited the fact that the U.S. Army provides for its men 131 gm. of protein daily and the Navy

* Those who favour a high intake of protein argue that protein by its specific dynamic action stimulates metabolism and gives the animal vigour and boost. This happens only when there is excess of protein to burn. Against this, Booher argues that this very fact of speeded-up metabolism accounts for the fact that the "Eskimos are short-lived, mature early and age quite young." In her opinion Chittenden's stand has not been proved untenable."

with 109 gm. (47). To harmonize the different recommendations about protein intake, Spiegel-Adolf (1945) suggests that there are three levels of protein requirements: (1) The minimal or emergency level, 18 to 40 gm. daily, barely sufficient for life and health, at least for a restricted time; (2) the average level of 70 to 80 gm. recommended by the National Research Council and (3) the optimum level of 110 to 140 gm. (47). Though there is some controversy about the protein needs of adults, there is general agreement that infants and children, pregnant women and lactating women require greater amounts of protein. Infants have a relatively larger body surface and growth is more rapid during infancy; 3 to 4 gm. of protein per kg. of body weight has been recommended for infants under 1 year.

The pregnant woman needs more protein on account of her increased metabolism, storage of nitrogen, growth of the uterus, growth of the mammary tissue, fœtal growth and repair and the hormonal preparation for lactation. During lactation, successful breast-feeding depends upon a proper protein intake. Nutritional authorities recommend 1·5 gm./kg. during the latter half of pregnancy and 2 gm./kg. during lactation. The Food and Nutrition Board of the American National Research Council recommends 85 gm. during the latter half of pregnancy and 100 gm. during lactation. The Indian nutrition experts recommend 101 gm. for pregnant and 112 gm. for lactating women.

For the aged, Tuchy (1943) observes "we may put down then, as our first duty to the aged, teach them the importance of protein and how to get their quota, no matter how old they are, 1 gm. per kg. of body weight" (50).

TABLE I

Recommended Protein Allowances

Recommended by the Food and Nutrition Board of America		Recommended by Indian Nutrition Experts	
Man (70 kg.)	70 gm.	Man (55 kg.)	82 gm.
Woman (56 kg.)	60 ,,	Woman (45 kg.)	67 ,,
Pregnancy (latter half)	85 ,,	Pregnancy	101 ,,
Lactation	100 ,,	Lactation	112 ,,
Children under 1,	3 to 4 gm./kg.	Children under 1	3·5 gm./kg.
1 to 3 years	40 gm.	,, 1 to 5 years)	
4 to 6 years	50 ,,	,, 5 to 7 years	3 ,,
7 to 9 years	60 ,,	,, 7 to 15 years	2·5 ,,
10 to 12 years	70 ,,	,, 15 to 21 years	2·0 ,,
Girls.			
13 to 15 years	80 ,,		
16 to 20 years	75 ,,		
Boys.			
13 to 15 years	85 ,,		
16 to 20 years	100 ,,		

How to secure our protein quota?—The next question is, how shall we get our quota of protein? In this regard, the advice of Baylis was, "Take care of the calories and the proteins will take care of themselves." Booher observes, "It has been proved as nearly as the science of nutrition and physiology *can prove anything*, that if the calorie requirements are adequately covered by common, staple protein-containing foods the protein needs for maintenance *at last* are also adequately covered and a liberal margin of excess food protein is simultaneously provided." But this applies to a mixed diet and may not be quite true of a strictly vegetarian diet. It is therefore, better to give a specimen diet which fulfils these needs. If we consume 9 oz. of rice, 5 oz. of bajri (or wheat), 3 oz. of pulses, 6 oz. of non-leafy vegetables, 8 oz. of green leafy vegetables, 4 oz. of milk, 2 oz. of oil or ghee and 2 oz. of sugar, we get about 2800 calories and 73 gm. of protein. This diet meets also our vitamin and mineral requirements.

Biological value.—The next important question is, are all proteins of equal value?; apparently not. The proteins of animal origin are more valuable to the body than vegetable proteins. Though both types of protein are equally digestible, they are not equal in their biological or growth-promoting value. At the top of the list among proteins of high biologic value stand those of milk. Meat proteins come next and lowest in the scale are plant proteins ([7]). According to Liu *et al* (1932), animal protein is twice as effective as vegetable protein in the maintenance of normal plasma protein levels and in the prevention of nutritional œdema ([53]). On the other hand the studies of Weech (1942) and Madden and Whipple have shown that certain vegetable proteins (*e.g.* yeast or bran flakes) are superior to animal proteins, *e.g.* beef, in stimulating the formation of plasma protein ([51]).

Bacharach and Macræ (1948) are of opinion that the traditional classification of animal protein as first class and vegetable protein as second class is inaccurate. They emphasize the fact that the proteins of green leaves and yeast, and the proteins of the embryo and the outer coat of cereal grains rank as high as some animal proteins. Though some plant proteins like gliadin of wheat and zean of maize are deficient, we have to remember that most foods contain more than one kind of protein and a deficiency of one protein is corrected by the other. Wheat for instance contains other proteins than gliadin, namely gluten and the proteins of the bran and the germ. These compensate for the deficient gliadin. The proteins of soya-bean, peanut and cotton-seed flours are excellent supplements for correcting the deficiency of patent wheat flour. Mixtures containing 5 parts of any of these flours and 95 parts of wheat flour have a definitely greater growth-promoting value. When 5 parts of milk powder are added, there is 157% more growth than on wheat flour alone. Wheat germ and corn germ stand

foremost among plant foods. The nutritive value of wheat germ protein is, in some respects, nearly equal to that of meat and milk. When fed at 10 per cent level, wheat germ was found to be as efficient as skim milk powder (28). In fact, it is possible to combine animal and cereal proteins to give a mixture with a biological value exceeding that of either (42).

There is a lamentable lack of agreement among investigators about the biological values of food-proteins; for example, the proteins of milk are given a biological value of 100 by Thomas, 74 by Bricker *et al*, 62 by Sumner and Marlin, 51 by Martin, Robinson and Lintzel, and 43 by Lintzel and Bertram. Even in the same laboratory *viz.* Murlin's, the biological value of the protein of whole egg for adult human subjects has been rated at 56, 92 and 102. Mitchell (1948) offers the following estimates of the biological value of a few food proteins for human adults, based upon all available information :—Whole egg 78, milk 78, meat 72, soya bean flour 65; rolled oats 60; whole wheat 55; corn meal 43; peanut flour 42; white flour 41(42).

How much of animal protein then should our diets contain ? The Indian nutrition experts advise, "This proportion may with advantage be one-third, preferably it should not be less than one fifth," Bethel and his associates (1939) found that when pregnant women consumed 50 gm. or more of animal protein, they did not suffer from anæmia but the incidence of anæmia rose rapidly with increasing deficiency of animal protein and reached 40% when the daily animal-protein-intake was below 30 gm. (53). On this basis, our pregnant women should take at least 25 ozs. of milk and preferably twice that quantity every day. But this is an ideal almost impossible to attain. I therefore, present to you the following observation of Sherman, "Several studies in man have shown that nitrogen equilibrium and apparent good health are obtained only when about one-tenth of the total protein in the diet is of animal origin" (39). I will also quote another interesting experiment. Levinson and others carried out experiments on human beings to determine the value of a vegetable protein diet. Their studies showed that (1) the vegetable protein diet is adequate in maintaining the serum protein, albumin and globulin as well as the hæmoglobin of the blood; (2) the antibody level of the blood as determined by the typhoid antibodies was adequate and there was sufficient protein in the vegetable diet to maintain this level; (3) there was no evidence of anæmia in the human subjects during the course of the experiment; (4) the weight loss was minimal, and there was absolutely no interference with the subject's work or daily routine and well-being; and (5) there was no manifestation of subclinical or chemical changes indicative of a dietary deficiency (35).

These facts indicate that animal protein is not superior to vegetable protein, as we have believed for a long time. Let me cite

two experiments showing that vegetable protein is, if at all, a little superior to animal protein. The first experiment was described several centuries before Christ. It is stated in the Old Testament that Daniel and his friends refused to take the meat and wine offered to them by the Master of eunuchs in the court of King Nebuchadnezzar and asked for "pulse to eat and water to drink". The Master of eunuchs agreed to try the experiment for ten days, "at the end of which their countenances appeared fairer and fatter in flesh than all the children which did eat the protein of the King's meat"(11) The second experiment was reported by Patwardhan and others in 1950. They found that when their human subjects were given a mainly vegetarian diet containing 11 per cent of animal protein, as milk, they retained more nitrogen (1·79 gm.) than when they were given 46 per cent of animal (milk or milk and egg) protein from which they retained only 0·84 gm. of nitrogen. They further found that the biological value of proteins in the basal diet varied between 39 and 53, but when the diet contained 46 per cent animal protein the biological value was much lower *viz.*, 26 and 41 per cent. They do not jump as I am inclined to do, to the conclusion that animal protein is inferior to vegetable protein, but cautiously suggest, "The finding that the protein mixture derived mainly from vegetable food possesses a higher biological value than proteins of a mixed diet with large amounts of animal proteins, is contrary to the general observation that animal proteins have a higher biological value than vegetable proteins and must need an explanation" (29).

I venture to suggest that about 10 gm. of animal protein would be quite adequate for an Indian adult and non-pregnant female. This may be easily had from 8 oz. of buffalo's milk.

Protein deficiency.—What will happen if the protein requirements are not met, and the protein supply is deficient? A deficit of protein can occur from a variety of causes:—deficient intake, a failure of absorption or utilization, abnormal destruction, or an abnormal loss from the body as occurs in burns or nephrosis (18).

When too little protein is supplied there is stunting of growth; children become emaciated and occasionally show some œdema which is however, less marked than in adults. Even when the deficiency is made good and they regain their average weight, they are still under-height for their age(16). Lynch and Snively (1951), have recently described a syndrome which they call hypoproteinosis, in children and infants. The symptoms include anorexia, failure to gain weight, gastrointestinal disturbances like vomiting and constipation, frequent bouts of infectious disease, dental caries and anemia. This is mild protein deficiency and is diagnosed by a proper dietary history(40). Kwashiorkor, a deficiency disease found in African children is due, according to the most recent findings to a protein deficiency(22). But growth is not the only consequence of

protein utilisation. Proteins are essential also for maintenance, and for a variety of stress-periods of maturity such as pregnancy, lactation, trauma, infection, intoxication and the like. As a result, over and above the weight-loss which is one of the best indications of protein deficiency, there are associated pathologic effects as muscular weakness, anæmia, leukopænia, hypoproteinemia, impaired lactation, decreased capacity to form antibodies, decreased resistance to infection, slow wound healing, lymphoid depletion and a reduced ability to fabricate certain hormones and enzyme systems([15]).

We will now consider a few specific instances: pregnancy is a period of metabolic stress. Deficiencies in the protein content of the diet of the pregnant woman may lead to nutritional œdema, predispose to toxæmias of pregnancy, give rise to anæmia and lower the resistance to infection. In two groups of women, a control group on a diet of their own choosing, and a study group receiving 110 gm. of proteins, it was noted that toxæmia and mild hypertension were four times more frequent in the control group; œdema was five times as frequent, preeclampsia eight times as frequent([53]).

Bertucci (1945) reports that there is a significant relationship between maternal morbidity and the protein content of the maternal diet. The morbidity in the deficient group was five times that in the excellent group([8]). There is a direct relation between the amount of protein in a mother's diet and the start in life she gives her infant. This relationship is of such magnitude that it can be demonstrated with each 10 gm. protein difference in the antepartum diet. Burke, Hardinge and Stuart (1943), are of the opinion "that less than 75 gm. of protein daily during the latter part of pregnancy results in an infant that will tend to be short, light in weight and most likely to receive a low pædiatric rating in other respects"([13]).

Let us now consider the relation between deficiency and lowered resistance. The association between war, famine and infectious disease, notably tuberculosis, enteric, and respiratory infection is common knowledge. This susceptibility to infection is a result of hypoproteinemia. Cannon, found that hypoproteinemia was common in cases of chronic disease, of whom those with total serum protein values of approximately 5 gm. or less per 100 cc. succumbed to a severe terminal infection([14]) Cannon postulates that due to a depletion of the bodily protein reserves, the capacity to fabricate antibodies is lost. He has cited evidence to show that many specific antibodies are present in the gamma-globulin fraction of the blood serum. He has also shown experimentally that protein depletion lessens an animal's capacity to fabricate specific antibodies and to resist induced bacterial infection and that this capacity can be re-established by dietary repletion with high quality protein. "Since antibodies are proteins, there seems to

be no other mode of antibody synthesis, except from dietary protein. This leads to the obvious conclusion that the consumption of an adequate diet is a *sine-qua-non* for protein repletion if acquired resistance is to be maintained "([15]).

Protein deficiency is of great importance also in surgical patients. An increased urinary excretion of nitrogenous products following injury (particularly fractures and major burns)–major operations and serious acute illnesses has been demonstrated by many investigators. The negative nitrogen balance in the first ten days following a fracture of the leg may amount to as much as 137 gm. of nitrogen ; equivalent to some 856 gm. of protein([18]). Loss of protein through the skin in patients severely burnt may be as much as 39 gm. of protein per diem ([45]). In these cases even diets of high calorie-value and of very high protein content fail to prevent a negative nitrogen balance at the beginning. It is therefore, advisable to begin a high protein diet when the catabolic phase is diminishing, around the 5th or 6th day. Cuthbertson recommends a protein intake of about 150 gm. per day([18]).

The proper healing of wounds also depends on adequate protein intake. Experiments in dogs and rats have shown that wounds and fractures healed significantly slowly on a low protein diet. Meyer and Kozoll (1944) have made similar observations in man. Spring (1946) reports that "even the largest bedsores we have seen among our patients with spinal cord injuries healed rapidly", when the negative nitrogen balance was converted into positive([31]).

Co-Tui (1946) found that in post-gastrectomy cases, those on a low nitrogen intake had a negative nitrogen balance, all had lost weight, their ergographic performances were poor, and their bed period averaged 22 days ; while all those on a high nitrogen intake were in positive nitrogen balance, gained weight, had superior ergographic performances and got out of bed in 12·5 days on an average([17]).

We thus see that the consequences of a protein deficiency are dire, but fortunately for us, they are reversible, requiring only a suitable repletion diet.

Diagnosis of Protein Deficiency.—"Protein deficiencies are actually of frequent occurrence in clinical medicine, yet they are seldom recognised because we as physicians are apt to view an inadequate protein intake with complacency. We have been lulled into a false sense of security by the supposition that there are large stores of reserve body-protein and that the absence of protein intake may result in little or no difficulty"([24]).

Both Cannon ([15]) and Ancel Keys (1946) attach great significance to weight loss ([30]). Youmans([54]) however, is of opinion that œdema is about the first clinical sign of protein deficiency. The œdema is usually painless, bilateral, and develops insidiously. This œdema masks the loss of weight. Polyuria, especially nocturia may occur.

Anæmia, weakness, and pallor occur later, as associated abnormalities. Youmans further believes that the determination of plasma proteins is a very valuable laboratory test of protein deficiency, and he attaches greater importance to the actual values of serum albumin and globulin rather than to the ratio of the one to the other.

The total plasma proteins at birth are 5·5 gm. per cent. of which 3·8 gm. are albumin and 1·7 gm. are globulin. At two years the values are 7·0 gm.% total proteins of which 5 gm. % are albumin and 2 gm. % are globulin. These values do not alter with age (34). These values have also been determined in the case of Indians by Datta (19), Menon *et al* (41) and by Gokhale and Chitre (26). There seem to be slight discrepancies due to different methods used by these investigators. But if we take the mean of the values of these workers, considered together, we will get values very similar to those of foreign investigators *viz.*, 7·0 gm. per cent total proteins, 4·5 gm. per cent albumin, and 2·5 gm. per cent globulin.

According to Moor and van Slyke (1930), œdema usually appears when the total protein falls below 5·5 gm. and the albumin below 2·5 gm. per 100 c.c.(43) Bruckman and Peters (19 0), give this critical level as 3 gm. per cent(12). Datta found that out of thirty cases of nutritional œdema, 25 had plasma albumin below 2·5 gm. per cent.(19) We can, I believe, safely take this as the critical level. In 20 cases of nutritional œdema, Gokhale and Chitre (1951) found 4·17 gm. of total protein with 1·53 gm. albumin per 100 c.c. (*Ind. Jour. Med. Sc.*, 4 : 398, Ref. : *Jour. Ind. Med. Assn.*, 20 : 267). It has been estimated that in chronic deficiency states, the ratio of fall in total circulating plasma albumin to loss of body proteins is 1 : 30. If the albumin falls from 4·5 gm. to 3·5 gm. per 100 c.c and if the plasma volume is 3000 c.c. in an adult, the loss in body protein would amount to 900 gm.(34)

It is fair, however, to repeat the warning note of Cannon at this stage, *viz.*, "Finally, unless all fractions of the plasma proteins are determined a diminution of one, for instance, albumin, may be paralleled by concomitant elevation of another, especially *beta* or *gamma* globulin, so that the total concentration of blood protein may again be within normal limits. Laboratory procedures therefore, although useful, should not be depended upon exclusively and indeed, may not furnish as much significant information as a careful dietary history and a record of marked loss of weight (15).

Treatment of protein deficiency.—A high protein diet is the obvious solution. But we have to remember that a patient chronically ill or convalescing from an acute illness requires a high calorie diet as well. While the healthy individual at rest may require about 2000 calories daily, the bed-ridden patient would need 3000 to 5000 calories daily.

The studies of Ravdin and Gimbel (1950) have shown that a nitrogen equilibrium cannot be achieved unless the protein is accompanied by non-protein calories. They found that at least 30 calories per kg. of body weight were required after major operations, so that the protein could be properly utilised (46). These should be supplied in the form of carbohydrates, lactose should be preferred to glucose as the latter is apt to give rise to distention. Carbohydrates should be given at the same meal as proteins so that the proteins may not be used up as fuel instead of building material (31). Cuthbertson recommends a protein intake of about 150 gms. per day in convalescence[18]. American and Canadian investigators have used with advantage as much as 300 to 400 gm. per day post-operatively or following injury (3). We should be cautious not to force this standard on an acutely ill-patient but wait for a few days. This diet should be selected from commonly used foods such as milk, meat, eggs, fish, cheese and should be given by mouth. According to Elman (1944), a convenient high-protein high-carbohydrate drink can be made up very readily by stirring 100 gm. of skim-milk powder into 200 c.c. of water. This furnishes 34 gm. of protein and 52 gm. of carbohydrate (23). Still higher quantities of protein *e.g.* 180 gm. may be indicated when there is great loss of weight. A case of burns involving 50 per cent of the body surface required 500 gm. of protein before healing occurred (20).

Allergy to protein.—We have talked of diseases due to protein deficiency. But protein may also give rise to certain disease manifestations due to hypersensitivity. These are infantile eczema, angioneurotic œdema, mucus colitis and bronchial asthma, which occur in this order with increasing age (33).

Proteins, vitamins, hormones and enzymes.—Considering the great significance of protein and the variety of its functions, it is but natural that it should have intimate relationships with other important substances like vitamins, hormones and enzymes in the body.

Riboflavin plays a role in the different enzymatic processes involved in protein-metabolism. The requirement of niacin is closely related to the type and amount of protein in the diet. In the absence of pyridoxine the desire for protein is lost. Protein is believed to spare pantothenic acid. Vitamin K is required in the synthesis of prothrombin which is a protein.(21)

Of the hormones, perhaps the growth hormone of the anterior pituitary exerts the most obvious effect on protein-metabolism. The adrenal cortical hormone is believed to control the rate of protein-catabolism and may also stimulate the formation of new protein. The thyroid hormone promotes protein-synthesis in the immature organism and there is gain in body weight. In the normal adult it accelerates protein-catabolism. It is believed to control the level

of serum globulins. Both androgens and œstrogens may exert an anabolic influence on protein-metabolism(52). Testosterone appears to increase the positive nitrogen-balance to the highest level on a limited calorie intake (6).

It has been found that during the preoperative treatment protein retention can be increased by administering methyl testosterone in doses of 25 mg. a day. The protein retention in such patients is frequently not reflected in weight-gain. But the clinical improvement, physical and mental, is as a rule sufficiently striking to leave no doubts as to its value(2).

Cortisone in doses of 100 mg. daily induces a slight increase in excretion of total nitrogen; larger doses such as 200 mg. induce definite losses. With ACTH (105 mg. daily) also there is no definite loss of nitrogen from the body. Both these hormones increase the catabolism of protein. The effect of these two agents on protein-metabolism may be related to the inhibition of hair-growth and tumour-growth in experimental animals, to the development of cutaneous striæ in human subjects and to the delayed healing of wounds which has been observed in animals and humans during the administration of these hormones (48).

Benditt (1947) has shown that at least these enzyme systems are intimately related to protein intake, *viz.*, (*a*) Pepsin and hydrochloric acid secretion of the stomach; (*b*) acid phosphatase activity of the kidneys; and (*c*) succinic dehydrogenase activity of the liver. All these enzymatic activities are definitely depressed in protein-depleted rats, and are restored to normal when protein is supplied (7).

Proteins and the secret of life.—According to Elman, "If there were any one secret of life, protein might well be considered as the heart of it since protein is the essential stuff of which all living tissue is made" (25). The line dividing Matter and Life dwindles almost to insignificance when we study the realm of viruses. The elementary bodies of vaccinia on the hand, are like small living organisms; tobacco mosaic virus on the other hand is a high molecular protein and has been purified and crystallised (32). We are thus faced with the challenging problem:—"Are viruses protein moleculars"? If they are all of this nature, then all life is merely a matter of shuffling and reshuffling of protein molecules. If they are not, what is it that makes them different? We do not know, and the mystery of life still eludes us.

Or consider this fact. Proteins may contain the same elements in the same percentage and still differ radically in their chemical, physical and physiological properties. Because of differences in their chemical structure some proteins—the toxalbumins like ricin and snake-venom behave as agents of destruction to health and life itself(28). You may call this a freak of nature or Divine Wisdom, just as you like.

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TREATMENT OF TYPHOID FEVER*

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SINCE I last wrote on this subject the treatment has been greatly revolutionised by the introduction of antibiotics, particularly Chloramphenicol, either the natural or the synthetic product. What was at one time a serious malady, with a long drawn-out period of sickness, has been brought under control. In this article, my experiences on the treatment of 107 cases of typhoid fever, treated with Chloramphenicol, in one form or another, are detailed.

I have been using Chloramphenicol from September 1949. These patients were all treated in the General Hospital in the Typhoid Ward. Till very recently, the use of this antibiotic was confined only to the serious cases, *i.e.*, cases which would normally have been declared as dangerously ill. In the pre-chloramphenicol days, an analysis of these cases, showed a mortality of about 45%. In this series of cases, the mortality has been reduced to 7·8%. The treatment with Synthomycetine† was restricted to the serious cases only, and at the present time, our experience of Synthomycetine therapy is largely based on the very seriously ill-patients. This drug Synthomycetine was exclusively used in my wards for last 9 month.

The drug is marketed as 0·25 g. capsules in bottles of 12. The recommended dose is to give 12 capsules, administering 1 capsule at intervals of a few minutes, and completing the 12 in about 15 or 20 minutes. In the first case there was undue sweating, and the appearance of a shock-like state was alarming to see. Thereafter, this massive initial dose was not attempted. Now, in my wards, it is only given 4 or 6 capsules stratum and thereafter 1 capsule 2-hourly or 2 capsules 4-hourly for the very toxic cases. In less toxic cases, it is given as 1 capsule 4-hourly. The drug is rapidly absorbed from the gastro-intestinal tract and is non-toxic, even in massive doses. In this series of cases, it is observed that if the patient was conscious before administering the drug, he remained conscious without going into the typical typhoid state. If the drug is given in the earlier phase of the illness, *i.e.* prior to the 10th or 14th day of the illness, it takes about a week for the temperature to settle down, but if administered in the third or fourth week, the temperature settles down in as short an interval as 24 hours and runs normal. This was observed in quite a number of my patients, as many of them used to spend 3 to 4 weeks at home before they thought of hospitalisation. As most of these patients were general ward patients, they could not afford to go in for this costly drug outside, even if it had been suggested to

* Specially contributed to THE ANTISEPTIC

† Synthomycetine is the synthetic form of Chloramphenicol manufactured by Messrs Lepetit & Co.

them by practitioners. The drug has to be continued even after convalescence has set in, for at least a period of 10 days, with a reduction in dosage In my own ward, once the temperature settles down to normal, patients are given 1 capsule 4-hourly for 3 days and then for the remaining 7 days, 1 capsule t d.s. With this treatment, relapses are cut down to a considerable extent. The relapse rate is high in cases treated with inadequate doses and also when Synthomycetine was stopped too early. So, to prevent relapses, the drug must be continued during convalescence. With this schedule, on an average 3 to 4 bottles will be necessary (9 to 12 gm.), but in very severe cases 8 bottles may be necessary, *i.e.*, 18 to 27 gm. of the drug. In none of the cases, was any anæmia or hemopoietic dysfunction observed. To my knowledge, no erythropoietic disturbance was observed in this Hospital in the last 4 years. The complication met with most frequently was occurrence of relapses in 8% of cases. The longest period after which the relapses occurred in my series of cases, was 18 days, but in the case of one of my colleagues, it was 28 days. The relapse rate used to be high in the early periods of our starting the treatment with Chloramphenicol. If we continued the drug well on into convalescence, practically no relapse occurred. In addition to use of chloramphenicol, Typhoid vaccine has been used in very small doses in my ward. I have observed that administering 1 million units subcutaneously daily, even when the temperature is on, has a very favourable effect. When once the temperature has been brought under control, the dose of vaccine is increased to 5 millions, 10 millions and then 20 millions per c.c. subcutaneously, every fourth day. This treatment practically cuts out relapses. In a small percentage of cases, where the relapses occurred even in spite of this continued administration of Chloramphenicol and typhoid curative vaccine, the relapse was very mild and generally ran a very mild course. Generally, we were able to control the fever in 3 or 4 days. In this series of cases, I did not lose even a single patient due to relapse. It should be remembered Chloramphenicol has only a bacteriostatic effect. The ultramicroscope studies has shown a bactericidal effect as well. But, our clinical experience so far, and the effect on carriers suggest that Chloramphenicol has largely a bacteriostatic effect only. Hence, the patient who is getting Chloramphenicol should be treated with as much care as if he is not getting any specific drug. Now although the advent of Chloramphenicol has proved to be a great blessing for the enteric cases, by no means can this be called a specific. Though the mortality has been reduced considerably, it has not been abolished by the advent of Chloramphenicol. What has been achieved by this is to cut down toxæmia to a considerable extent. If the patient is admitted sufficiently early, practically no toxic symptoms as typhoid state, perforation, hæmorrhage, meteorism, are observed.

Total No. of Cases observed	...	107
Treated with Chloromycetin*	...	47
Treated with Synthomycetine†	...	31
No antibiotic	...	29

Total No. of Cases treated 107

Chloromycetin		Synthomycetine		No Antibiotic	
Cured	Died	Cured	Died	Cured	Died
43	4	29	2	25	4

Besides relapses, the next serious complication as a result of chloramphenicol therapy, is the production of raw tongue and stomatitis. This is particularly seen in patients whose general nutrition is already poor. Though this is troublesome, it is easily controlled by giving those patients gargles with Potassium permanganate 1 : 1000 and crude liver extract parenterally and vitamin B complex orally. This condition is particularly likely to occur in patients who have been on chloramphenicol for much longer than 3 to 4 weeks. In other words, it is more commonly seen in patients suffering from infections other than enteric, where they are mistakenly diagnosed as enteric and treatment with chloramphenicol is persisted in expecting the temperature to settle. I have seen this in a case of kala-azar where the patient was administered chloramphenicol for over a month. Occasionally we have seen it even when chloramphenicol had been administered for shorter periods. This is in common with other broad-spectrum antibiotics which interfere with the intestinal organisms. Luckily it is not a more common event.

The next common complication is diarrhœa. Patients have loose bowels during the administration of chloramphenicol, but diarrhœa is never so severe as when it occurs as a complication of typhoid itself. Diarrhœa, due to fever, is much more severe and is exhausting to the patient and it also indicates the high degree of toxicity, whereas when diarrhœa is met with in the course of treatment by chloramphenicol, it is generally milder and the patient himself is not toxic. The diarrhœa can also be controlled by administering at the same time kaolin up to 3 ozs. in 24 hours. The diet can also be reduced to a non-residue diet, like arrow-root *kanji* and citrated milk. If diarrhœa is at all troublesome, milk may be altogether avoided or skimmed buttermilk may be given. Generally, when diarrhœa occurs, meteorism is also likely to be seen in a case of typhoid. But when diarrhœa is occurring, in the course of chloramphenicol administration, the meteorism is not so pronounced or is even absent altogether. If meteorism is at all observed, it can be quickly controlled by giving turpentine stupes and turpentine enema or combining the administration of essential

* Chloromycetin is the trade name of Chloramphenicol marketed by Messrs Parke Davis & Co.

† Synthomycetine is the trade name of Chloramphenicol marketed by Messrs Lepetit & Co.

oil mixture, but in none of my series, was meteorism observed when the patient was on chloramphenicol. Another complication that is met with, is a certain amount of peripheral neuritis, particularly at the time of discharge. Stomatitis and glossitis are more likely to be seen, if by any chance the capsule is not intact. Though chloramphenicol itself produces diarrhœa, I have used it in typhoid cases with diarrhœa, with considerable benefit. In these cases, instead of worsening the condition, the diarrhœa was brought under control. Yet another complication met with is delirium. In this series, it was present in 9% of the cases. Of these, 50% died. So, delirium occurring in typhoid should be taken as a serious symptom. The other serious complications are perforation, hæmorrhage, hæmoptysis, peripheral failure, bed sores and coma vigil. The effect of administration of chloramphenicol is first noticed when the toxicity of typhoid fever is controlled. In the first 24 to 48 hours, the typhoid state clears, *i.e.* the clouding of the mind clears first. In the clearing of the clouding of the mind, the anxiety that the attending physician has regarding his case, also clears. This is what is seen in the large majority of toxic cases. If this does not occur, then the case should be considered as too toxic and more energetic treatment must be thought of. After the toxicity clears, complications if any, like hæmorrhage or meteorism or diarrhœa are quickly brought under control. As already mentioned, the temperature is brought under control. In my series of cases, it varied from as short an interval as 24 hours to as long as 7 or 8 days. The longer the period for which the patient survives after chloramphenicol has been started, the better seems to be the prognosis. Cases that are lost are those in which the drug had not had sufficient time to act, *i.e.*, we generally lose patients within the first few days after admission. The toxæmia can be controlled very well, by administering plenty of fluids, either orally, or if this route is not feasible, by a continuous rectal drip. Normal saline can be used, 5 to 6 pints in 24 hours. Even without the antibiotic, this procedure alone is capable of controlling the toxæmia.

In a series of 10 cases, I used Cortisone along with Synthomycetine. Two of them died. In the first case, the man had already developed peripheral failure when I started him on cortisone tablets. The administration of cortisone tablets, cleared the toxæmia and pulmonary œdema and brought down the temperature, and the patient improved considerably. He was a labourer and could not afford to continue cortisone indefinitely. He died on the fourth day after having synthomycetine and cortisone only for a short time. The improvement noted in the man was so dramatic, that although we ultimately lost him, it made me try cortisone wherever it was possible. The dose I have employed of cortisone should be considered almost homœopathic. I have given only one tablet of 25 mg. t.d.s. for the acute period and as soon as the

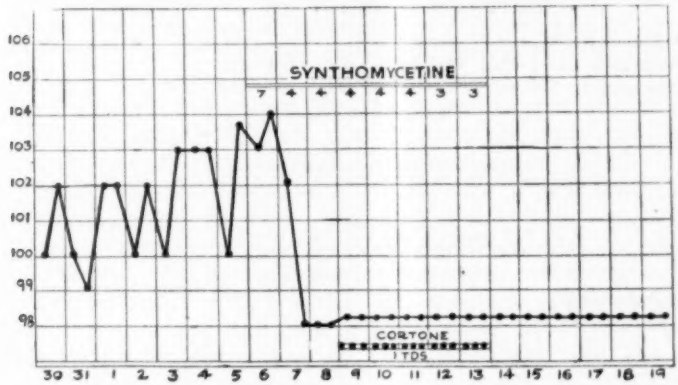
toxic process had been brought under control, it was reduced to ½ tablet t.d.s. then ¼ tablet t.d.s. before finally stopping the same. The second case was of an young girl of about 18 years, also a poor patient and I used cortisone tablets made available by the courtesy of Messrs Merck. In this case also, I did not give full doses, but only 1 tablet t.d.s. for 2 days and though there was a slight initial improvement, the patient steadily got worse and died. She was in the typical typhoid-state and was not touched by cortisone therapy. I feel that if the dose had been much larger than what I gave, both cases might have survived. I have combined this therapy in 2 cases of typhoid perforation. Both of them were saved and the post-operative course looked as if a normal abdomen was opened and closed. Within 24 hours after operation, both of them were maintaining normal temperatures and no relapse occurred in either of these cases. The condition of the patients at the time of discharge was extremely satisfactory. They did not present the pitiable, thin and emaciated appearance of most typhoid patients at the time of discharge. In the other cases of the combined administration of cortisone and synthomycetine, the results were dramatic. In nearly all of them, the temperature settled down in less than 24 to 48 hours. The administration of cortisone seems to raise the resistance of the individual and the administration of synthomycetine favours the body resistance, preventing the multiplication of the typhoid bacilli. Hence, this combination gives extraordinarily good results. The great objection is the cost of the drug. Personally, I would prefer 2 tablets of cortisone of 25 mg. each, to be given t.d.s. on the first day, and the full dose of synthomycetine as advocated, to start with. If this regime can be employed, the temperature should be controlled in 24 to 36 hours. In 2 cases, in place of cortisone, I used ACTH. This also appeared to give as favourable a response as cortisone. A much larger series of cases should be tried with this combination. The only objection to this combination may be, apart from the cost, the danger of allowing the patient to be ambulant too soon. For this, my only answer is, it is much better to restrict the man's activity and keep him in bed after he is completely normal than to have a sick man on hand and be looking after him. The administration of this combination has taken away much of the fear that typhoid normally produces.

In case of hæmorrhage, where Chloramphenicol was used, the hæmorrhage continued for nearly 2 days in spite of his getting the specific drug This only shows that the drug has no action on the course of the disease, but only exerts a bacteriostatic effect on the causative organism. If hæmorrhage occurs, it has to be treated on the same lines, as if the patient was not getting Chloramphenicol, *i.e.* he should be given blood transfusion, if at all the hæmorrhage is severe and morphine ¼ grain and atropine $^{1}/_{100}$ grain given intramuscularly to allay the anxiety of the patient or congo-red 1% solution 15 to 20 cc. can be given intravenously. It is also advisable

to give liquid diet, preferably iced. If the bowels do not move for 2 days after the hæmorrhage, a glycerine enema may be given.

TEMPERATURE CHART—I

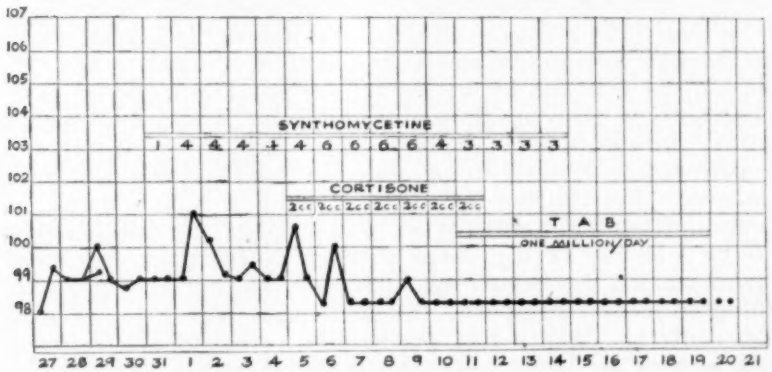
Patient's Name: N., age 20 years. Labourer.
Date of Admission: 30-12-'52. Widal + ve 1/200.
Date of Discharge: 20-1-'53. Blood culture for B. Typhosus, + ve.



Till the advent of Chloramphenicol, typhoid perforation meant a very bad prognosis even with operation. For one thing, these cases are not spotted in time, and even when spotted, it takes some time before the patient is submitted to an operation. Then the risk attendant upon the operation is also there. Now with the advent of Chloramphenicol it looks as though perforation is more commonly

TEMPERATURE CHART—II

Patient's Name: P., age 24 years.
Date of Admission: 27-1-'53. Widal + ve 1/200.
Date of Discharge—19-2-'53. Blood culture for B. Typhosus + ve.

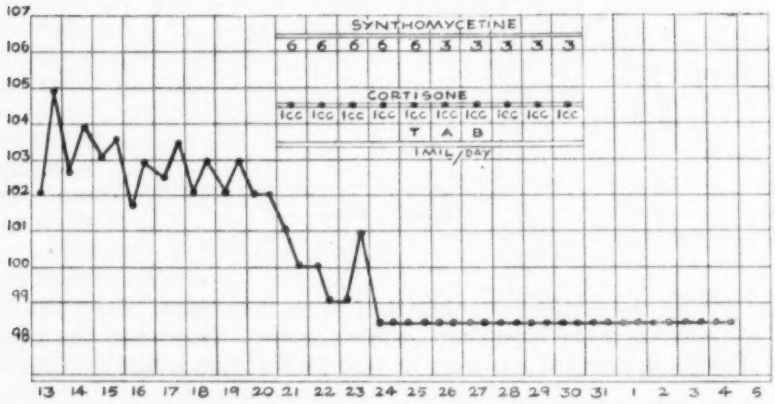


seen, *i.e.* because these toxic cases in the pre-chloramphenicol days would not have survived. Now they are not only able to withstand the perforation, but also go through the operation successfully and survive. The survival is made possible, not only by the operation

but also by controlling the toxæmia by cortisone and controlling the infection of the peritoneum by synthomycetine. It is interesting to note that in the same period, even in the cases which were not given the antibiotic—29 cases—the mortality was 4 *i.e.* 13·7%. These were all cases which were clinically judged to be mild cases of typhoid.

TEMPERATURE CHART—III

Patient's Name: Mr. R., age 17 years.
Date of Admission: 13-1-'53. Widal (16-1-'53) + ve 1/100.
Date of Discharge: 5-2-'53. Widal (18-1-'53) + ve 1/200.
Blood culture: Sterile.



Going through the Hospital records for a number of years, less than 1% of cases of perforation survived, with operation in the pre-chloramphenicol days, and none without operation. In the case of perforation, if the patient refuses operation, then the same can be treated by stopping all fluids by mouth and administering only synthomycetine capsules at the rate of 2 caps. 4 hourly and maintain the nutrition by intravenous drip. The intravenous feeds should contain glucose, protein hydrolysate, vitamin C 1000 mg. per day, and nicotinic acid 300 mg. per day. By this procedure, the perforation is likely to get sealed of itself and the case is likely to recover. For the first few days, distention might occur. The distention itself will gradually be brought under control by stopping all feeds. In one of my cases without perforation, very troublesome distention was occurring. In this case, by completely withholding all feeds by mouth, the distention was rapidly brought under control. Agents like pituitrin or carbachol are contra-indicated, as they are likely to cause violent peristalsis and precipitate perforation.

With regard to the diet of typhoid patients, I do not believe in starving them. I allow them arrow root *kanji* 2-pints per day, sago *kanji* 2-pints and well-skimmed buttermilk 2-pints. In

addition, they are given orange juice or tomato juice, 6 to 8 ozs. If there is no distention, glucose may be added to the *kanjis* as well as to the fruit juices—up to 3 ozs. When there is distention it is likely to be made worse by adding glucose too liberally. This diet agrees very well in uncomplicated cases. The calorific value of these fluids is about 1500 calories, but if there is any diarrhœa, diet is restricted to albumen water and arrowroot *kanji*, *i.e.*, diets with no residue. With such a no-residue diet, diarrhœa is quickly brought under control. Once the diarrhœa is controlled, other *kanjis* may also be given cautiously. If the motion shows curdy precipitates, it means milk is not digested well and that it would be better to use citrated milk. Citrating of the milk is done by adding 2 grains sodium citrate to each ounce of the milk feed. For cases with constipation, a slightly more liberal diet may be given. This diet is maintained till the temperature touches and maintains normal. For the first 3 days of the afebrile period, no alteration in the diet is made; after that, the diet is slowly increased by including, to start with the soft portion of the bread boiled in milk feeds, custard and mashed potatoes. This is given for 3 more days and from the sixth day of convalescence onwards, double boiled rice and curds are given. During the fever period itself, I give in uncomplicated cases, shark liver oil emulsion 3 ozs. a day. Each ounce of the emulsion contains 2-drams of shark liver oil. This by itself gives 600 calories per day. The result of this is, the patient gets quite a good number of calories in a small bulk. I have examined these patients' motions and I have not seen either the fat or the oil globules, showing that the oil had been completely absorbed in the intestinal tract. The idea of giving shark liver oil emulsion is not only to supply the calories, but also to supply Vitamins A and D in good amount. By adopting this treatment, I have observed that patients are not emaciated at the time of discharge. In pre-chloramphenicol days, the course of typhoid fever was a very prolonged one, and dieting was all important. We did not want a man who was suffering from prolonged fever to be starved for a long period. With the advent of Synthomycetine however, the fever period has been considerably cut short and one need not now bother to the same extent about the calorific value of the diet.

The incidence of parotitis has practically disappeared with the introduction of Chloramphenicol—I have not had any case for the last 9 months, *i.e.* the period in which the drug was put into to use more liberally than before, due to the generous supply of the same, but prior to that, I used to see this complication occasionally and in these cases, if the complication was seen sufficiently early, it could always be averted by giving 3 to 5 lakhs units of Penicillin as injection. If, for any reason, the case has come late to the hospital or the earlier phases had been missed, then surgical incision and drainage is called for. At this stage, it may not be out of place

to point out the antagonism between Penicillin and Chloramphenicol. If, for some reason or other, Penicillin is to be given to a case of typhoid receiving Chloramphenicol, the dose of Chloramphenicol must be increased to at least 30% of the previous level to achieve any result. There seems to be some specific antagonism between Penicillin and Chloramphenicol.

Carrier states:—Fortunately, during the last 1½ years, *i.e.* with the advent of Chloramphenicol, we have not had any case of typhoid carriers—probably, due to the fact that the organisms are completely brought under control by Chloramphenicol and the natural defence organism of the body, but in the literature it is stated that the carrier state is not considerably cleared by administering Chloramphenicol. All the same, it is worth administering massive doses of Chloramphenicol for short periods and observing the effect of the same. It has been said, administering orally 3 doses each of 4 gm. of soluble Iodothaline at 3 day intervals as used for Cholecystography, brings about a cure. Cholecystectomy is also supposed to result in a cure in 75% of the intestinal carriers.

The following few cases are recorded to illustrate some of the noteworthy variations.

In case 2 (A.K.) the temperature was not controlled by the antibiotic and the temperature persisted for 24 days in spite of the antibiotic. In this case, blood culture was positive, W.B.C. count was 12,600 per cm.m. and differential count was P. 70%, L. 20%, E. 8% and M. 2%. One possible explanation may be that the dose was perhaps too low. With an adequate dose, it is quite likely that the temperature might have been brought down quicker.

In 2 non-toxic cases, Chloromycetin took 5 days to control the temperature. In the first case (Case 30—K.M.), Widal was $^{1}/_{40c}$ positive against B. typhosus. Total W. B. C. count was 3200 per cm.m. and differential count was P. 70%, L. 14%, E. 8% and M. 8%. In the second case (Case 59—P.), blood culture was positive for B. typhosus. Widal was negative. Total W.B.C. count was 8200 per cm m. Differential count was P. 76%, L. 18%, M. 4% and E. 2%. Both these cases were non-toxic and yet the antibiotic took full 5 days to bring the temperature down to normal. Probably the defence mechanism of the body was itself getting the disease under control and the antibiotic was not as beneficial as in the more toxic cases. Even so, the temperature was brought under control in 5 days instead of the usual 4 to 5 weeks' time. In contrast to this, in 2 toxic delirious cases (Case 29—K.), Synthomycetine brought down the temperature to normal in 24 hours and along with that, the delirium also cleared. In the second case (Case 33—A.), Synthomycetine brought down the temperature to normal with 12 caps. Due to paucity of supply, the drug had to be stopped. For 10 days, the apyrexial interval lasted and then relapse occurred. Again, the temperature was effectively controlled. This case clearly

illustrates the need for maintaining the treatment during convalescence. An un-understanding administrative head may bring about hardship to enteric cases by stopping the supply of the drug too soon.

In one case (Case 47—M.), the blood, urine and motion were all negative for typhoid. The case was clinically quite typical of enteric fever. In this case, marrow culture was positive for typhoid. Subsequently, Widal was found to be $^1/_{400}$ positive for B. typhosus. Temperature settled down to normal in 8 days after starting on Chloromycetin. In case 55 (N.), the patient was very toxic and was in the state of coma vigil. Chloromycetin was administered. The effect was very dramatic. The toxæmia cleared in 48 hours and the temperature settled down to normal in 96 hours. Relapse occurred 12 days later. The relapse was running a mild course and was treated symptomatically.

In a case of perforation (Case 67—R.), the patient was admitted for acute abdomen. Laparotomy showed perforated typhoid ulcer with thick pus. The abdomen was drained. Thick pus continued to drain. He was put on massive doses of Chloromycetin. Despite the use of antibiotic therapy, the patient deteriorated and died six days after admission. It is in these sort of cases that cortisone is worth trying. The result might have ended favourably.

Case 70 (B.) illustrates the need for the clinician to be on the look-out for more than one infection operating in a case. In this case, the patient was non-toxic. He had enlargement of spleen and liver. Total W.B.C. count was 3600 per cm.m. Differential count was P. 54%, L. 42% and M. 4%. In view of this, sternal puncture was done and L.D. bodies were found. B. typhosus was also grown in a routine blood culture. He was treated with urea stibamine for kala-azar and Chloromycetin for typhoid. The result of the combined treatment was very satisfactory. It is worth while recording here that kala-azar is not affected by any of the antibiotics thus far available. I have come across cases in which 8 to 10 bottles of Chloromycetin, Synthomycetine, Terramycin and Aureomycin had been used. In one case, the temperature persisted for nearly 3 months and the patient was on one antibiotic or another all the time, without appreciable lowering of the temperature.

In case 71(R.I.), the total W.B.C. count was 2200 per cm.m. Differential count showed P. 32%, L. 65% and M. 3%. Blood culture—para-typhoid A was isolated. Agglutination for the same was 1/100. The patient was toxic from the outset. Both the temperature and the toxicity were controlled within 48 hours, by administering Chloromycetin. Hæmoptysis was present during the febrile period. The interesting features in this case were:—the toxicity in a para-typhoid case, extreme leucopænia and hæmoptysis. Case 84 (S.), is interesting in that the dose of antibiotic used was very small, *viz.* only 8 caps. of Chloromycetin. In this case, the blood culture

was positive for B. typhosus. Widal 1/40 agglutination against B. typhosus. Total W.B.C. count was 9600 per cm.m. Differential count showed P. 38%, L. 60% and M. 2% and no E. The temperature responded in less than 36 hours and no further antibiotic was used and no relapse occurred either. It is really strange that a case in which the blood culture was positive, should have responded so dramatically to such a small dose of Chloromycetin. The lowest total W.B.C. count recorded in this series of cases was 1900 per cm.m. The case in whichthe W.B.C. count was found to be so low as this was Case 88 (S. M.); the differential count was P. 63%, L. 35%, and M. 2%. The blood culture was sterile. Widal 1/200 agglutination against B. typhosus. The patient was not toxic and the use of antibiotic was not warranted. Temperature settled down to normal on the fourth day of bed-rest and hospitalisation. This is noteworthy in view of the extreme leucopænia. Generally, with such a low count, one expects the disease to run a bad course. The highest W.B.C. count recorded in this series was 14,000 per cm.m. in a toxic delirious case. So, evidently the W.B.C. count bears no relation to the course of a case.

Conclusion.—As this short paper will show, the introduction of Chloromphenicol, marks a definite advance in the treatment of enteric fever. Temperature is controlled in the large majority of cases in less than 5 days and relatively higher doses are indicated in toxic cases; in cases with delirium, particularly a high dose is indicated. Treatment should be carried on well into convalescence, for at least 10 days to prevent relapses. If the treatment is started sufficiently early, complications may be avoided. Cortisone combines freely with Chloramphenicol therapy. The sole objection that I can see, to the combination therapy, is the cost of the drugs. Till very recently, in all the enteric cases which were under my care and which received Synthomycetine the drug was supplied free by courtesy of Messrs Ranbaxy and Company Ltd., the agents of Messrs Lepetit & Co., I offer my sincere thanks to them and my patients are grateful for the timely supply of the drug.

I am thankful to the Dean of the Government General Hospital and to the Director of Medical Services for permitting me to publish this article. I am specially thankful to my house-physician Dr. M. P. Achutha Menon, M.B., B.S. for the labourious task of collecting the factual data of the cases presented.

References:—Subramaniam, R.—The Antiseptic, Aug. 1949.

Chlorophyll and Hospital Odours

The objectionable smells and odours associated with the nursing of the low grade mental defectives in hospital wards, were considerably reduced by giving the patients chlorophyll tablets of 100 mg. twice a day.—(Abst. in *Med. Jour. Austral.*, 13-12-1952 from *The Canadian Med. Assoc. Jour.*, July 1952).

STAMMERING—ITS CAUSE AND CURE*

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Introduction.—The language function is defined as the perception and understanding of the spoken and written word together with the expressive abilities of speaking, spelling and handwriting. Disorders in the development or efficiency of any part of this function may result in emotional conflict, social maladjustment and scholastic retardation. The converse, by no mean less frequent, is likewise true. Speech disorders are of two kinds :—(1) congenital or developmental disturbances which prevent or hinder the proper acquisition of speech ; and (2) deterioration which causes speech, though normally developed, later to become defective. We are here concerned with deteriorated or defective speech.

Defective speech may be of various types such as: (1) faulty articulation or lisping ; (2) Echolalia : here there is a parrot-like repetition of words spoken by others without understanding their meaning ; (3) Aphasia which is a disability in proper verbal expression (motor) or comprehension (sensory) ; (4) Psychogenic : here due to self-consciousness, speech becomes too rapid and complex, and as a result defective ; (5) stuttering or dysphemia, where there is more or less constant inability to speak freely. It is this type of defective speech which forms the subject matter of this paper.

Inability to speak freely may result in (*a*) a *stutter*, where there is repetition, in some cases slow, in other cases rapid, of a word or syllable before the following word or syllable can be uttered ; (*b*) or the speech may be *spastic*. Here there is a noticeable hypertonicity of the nerve fibres actuating the muscles used in speaking as well as a marked contraction of the facial muscles ; (*c*) or the speech may show *hesitation*. This is marked by a silent choking effort often accompanied by a fruitless closing and opening of the mouth ; (*d*) there may be a *stammer*. Here the person is unable to begin a word or a sentence and his effort to speak is accompanied by marked muscular contractions and pronounced spasmodic efforts resulting in all sorts of facial contortions, grimaces and uncontrolled jerking of the head, body and limbs ; (*e*) then there are cases of combined *stuttering and stammering* or there may be a combination or any two or more of the above described types.

All these different variations have the following characteristics in common. These patients can :—(1) sing without difficulty ; (2) talk normally when alone or when talking to animals ; (3) cannot talk and do something else at the same time ; (4) show an intermittent tendency *i.e*, there are times or periods when they can talk normally but these are of short duration and the trouble always comes back ; (5) the trouble cannot be outgrown ; (6) there

* Specially contributed to THE ANTISEPTIC

is a progressive tendency which becomes worse as the child grows older; and then it is more difficult to correct.

PATHOGENESIS.—Inability to speak freely is usually due to a defect anywhere in the peripheral speech mechanism, which consists of (1) the muscles of respiration—intercostals and diaphragm; (2) muscles of the larynx which control the vocal chords and glottis; (3) the tongue; (4) the soft palate; (5) jaws; (6) cheeks; and (7) lips. What takes place when there is inability to speak freely may be better understood if the process of normal speech is reviewed.

The voice box or larynx situated at the top of the trachea may be regarded as a wind-reed musical instrument which produces sound as a result of air being directed upon the reeds which consequently are thrown into vibrations producing a tone which will have pitch, length and steadiness in accordance with the amount of breath which has been taken and the control thereof. If it is allowed to escape before tone is initiated and continues to do so during its production the voice will be "breathy" or if the air is directed suddenly and forcibly against the reeds, the tone will be started explosively and the voice as a result will be harsh and unmusical. The "reeds" in the larynx are called the vocal chords and are wedge shaped bands which are not free anywhere except at their inner edge, being attached closely to the sides of the larynx. These chords are apart in silence. They approximate for the production of voice and this they must do, at the exact moment air reaches them in its outward and upward passage. When there is an inco-ordination here, stammering results. But stammering may also occur because though the vocal chords approximate, the quantity of air breathed is not sufficient to produce sound. Here the fault lies with the respiratory apparatus. That the muscles of respiration are at fault in the case of almost all stammerers has been proved, by measuring the vital capacity of the lungs of stammerers. This when compared with the normal for that particular person is found to be only half or two-thirds of what it should have been. Again examination of the stammerer under the fluoroscopic screen shows the movements of the diaphragm and the intercostals very sluggish, sometimes jerky and altogether abnormal, thus proving that the lung capacity for air is also below normal. Thus derangement of breathing is a major causative factor in stammering both as to the amount of air inspired and to the way in which it is taken and above all to the lack of control of it, and therefore as we shall see later, re-education and training of the muscles of respiration is a very important step in the treatment of stammering. This may be all that is required in early cases, but later on other muscles concerned start acting wrongly and these also have to be re-educated. These may be, as we said above, the closing muscles of the vocal chords, and the soft palate, which may be, and often is in these cases, spasmodic in its movements. Then again the tongue often becomes unruly to a degree

which is little understood. This is caused by the diaphragmatic spasm producing reflex spasms in the tongue. The most marked of these are at the back, retracting the entire tongue, almost closing the back of the throat and preventing the true emission of the voice. This brings about a fault in enunciation also—as it prevents the tip of the tongue from coming sufficiently forward in the mouth, both for the pure formation of vowels and for the clear articulation of consonants especially those which are formed by it and the hard palate just behind the upper front teeth. Then there is the clenching of the jaw which prevents the mouth from opening sufficiently to permit the voice to pass out freely. Faulty action is also present in the muscles of the cheeks and lips. Nasal insufficiency, though not a cause of stammering, may prevent cure. Stammerers are extraordinarily sensitive to any interference with either the free upward and outward passage of the voice or to the co-vibration which normally takes place in the nasal cavity. Any nasal impediments such as a deflected septum or adenoids should therefore be removed before a successful issue to treatment is expected.

Spinal curvatures, knock-knees, and flat feet are often seen in stammerers. This seems to cause an irritation and nerve tension and speech is very much benefited when these faults are corrected. Knock-knees and flat feet with their concomitant of faulty distribution of weight also contribute materially to and in some cases are the primary causes of faulty balance and general lack of co-ordination found in stammerers. The flattened ribs in scoliosis impede the expansion of one lung and bring about version of the diaphragm, causing the spasmodic irregular breathing of the stammerer. So also do other abnormalities in the framework of the thorax. In these cases, treatment should be started early by graded breathing exercises, to restore the contours of the thorax and thus bring about normal breathing with consequent marked improvement in stammering. We see from the above what exactly happens in stammering and how the peripheral speech mechanism is at fault. The causes of faulty action are mainly: (1) organic diseases of the brain; (2) psychogenic; (3) diseases of the peripheral speech mechanism; and (4) mimicry. The organic diseases of the brain usually blamed are encephalitis from various causes, meningitis, chorea, polio etc. These usually act affecting the speech centre in the brain. Any one of these may initiate the faulty speech, which if not corrected immediately is then kept up by the muscles concerned getting into the habit of wrong action. So also stammering may be initiated by disease affecting any part of the respiratory tract and causing derangement of breathing which, if not corrected, may continue through force of habit of wrong action of the respiratory muscles. Mimicry as a cause of stammering acts also through force of habit. It is because of this that stammering is found running in families and has given rise to the mistaken idea that stammering is

hereditary. At most there may be a predisposing tendency which together with the imitativeness natural to children seems to be responsible for finding more than one stammerer in the family.

Lastly we come to the psychogenic causes of stammering. These may be a result of something psychical. A fall or an operation may not be responsible organically for the stammering and yet produce a psychological trauma which deranges normal breathing by throwing all the muscles of respiration, voice and articulation into confusion. The same thing happens when there is a psychological maladjustment in the family, as a result of a faulty parent-child relationship. So also checking left-handedness or thumb-sucking too drastically may result in stammering. Trying to cure stammering by ridiculing the child or beating it makes the condition worse, as it enhances the nervous factor so often responsible for the trouble.

TREATMENT:—The muscles concerned in speech must be trained separately and then co-ordinated and brought under the control of the brain. Next, the body as a whole is trained to ensure smooth controlled movements. Next study of good delivery and acquirement of good musical speech are undertaken. Side by side the underlying fears and nervous apprehensions must be overcome. In very early cases before wrong muscle action has become established, treatment of the nervous aspect alone may bring about good results. But this does not occur later on, except where the causative agents have been disasters such as concussion, nervous shocks of various kinds, etc.

In children, treatment should be started as soon as the trouble starts. It should not be delayed in the hope that it may be outgrown. These children are usually between 3 and 5 years of age and treatment should be started immediately the trouble starts. The history should be gone into very carefully for chest troubles, falls, operation etc , as well as maladjustment in the family. The habits and hygiene of the patient should be carefully attended to. Improper food and the habit of bolting it down causes indigestion and often brings back a stammer even after the wrong way of breathing has been corrected. The general health therefore must be optimum. Needless to say the child should not be bullied or teased, as this will only serve to perpetuate the trouble. After all this has been attended to, the active treatment should be started. This in the child consits in correcting the deranged breathing and psycho-analytic treatment if the causative factor is a psychogenic one. In the adult or when the case is of fairly long duration, in addition to correction of wrong breathing re-education of the muscles of voice and articulation will be required. Together with this will be the need to deal with the fear complex which in the adult will be deep-rooted and long established. Reflex spasms of the laryngeal muscles of the soft palate, tongue, jaw, face and lips will have become habitual.

Moreover when the stammerer finds himself unable to articulate a letter or word he usually tries to force it out, thereby making the lock still greater, and often breaking into a perspiration in his efforts. The entire body becomes rigid and he cannot let go anywhere, worst of all he is certain to have taken breath with a quick gasp, and the breath will have become jammed.

The first step in the treatment is to teach the patient to relax and this usually takes a great deal of time and work. Until this has been accomplished, no direct work on the stammer should be attempted; as the ability to relax is gained, it will almost imperceptibly merge into being able to "let the breath go," a thing which is at first incredibly difficult. Again and again it will be found that the stammerer has employed force to exhale and no progress towards normal speech will be possible, till the breath can be released without any trace of effort.

For correct speech, inspiration and expiration must go on slowly and smoothly, and it is useless to request the stammerer to speak on normal breathing till abnormality has been overcome. Then and not till then can work be begun to bring about the co-ordination between the muscles of respiration and voice which is always faulty and often completely lacking in the stammerer. This in most stammerers' clinics is achieved by the practice of singing long notes softly and smoothly on controlled expiration

The Rami method.—But in the cases I had watched being treated by Mr. M. S. Rami in his clinic at Bombay, a device invented by the doctor brings about correct breathing in a very short time, and obviates long hours of singing practice, which may be quite difficult in young children and in adults who have no ear for music. Besides, the course of treatment is cut short and the patient with the device in his mouth, starts immediately on the uttering of short sentences. The method followed by Mr. Rami was:—The first step in his treatment consisted of preparing a special device for each individual patient. The device is a light arc-shaped fixture which the patient puts on in such a way that it closes the palate completely. Then the patient is trained to press the tongue against the device from below in such a way that the entire breathing through the mouth is restricted to a small aperture in the middle of the device. All the breath-taking is done through the mouth and through the aperture in the device, and is done in a continuous inflow of air till the patient has stored enough breath in his lungs for a normal articulation of a period. This breath is then used to expirate a monosyllabic word which is unduly prolonged. After repeated practice the word to be uttered is a diplosyllabic one, and while articulating this word the first syllable is unduly prolonged in a sing-song way. Progressively the word practised next is of three, and then of four syllables. The next stage is uttering of short phrases and sentences—always observing the principle

that the breath taken in is finished by the time the "foot" of a certain number of syllables is uttered, and always seeing to it that the first syllable of this "foot" is prolonged.

From the point of view of timing, the practice starts with about 30 words per minute, this speed being increased gradually to 90 or 100 words, which is the speed attained by the patient at the end of a normal training. The patient is made to sit or stand at perfect ease and to relax completely. The articulation practice is done smoothly but firmly without any faltering of the voice. The pitch adopted is the normal one used in conversation, but during the reading lessons and elocutions it is raised to secure audibility.

On an average the patient spends about six to eight hours every day with the Director of the Rami Clinic in various types of exercises. Though reading out is the common mode of exercise, the patient also gets a chance of conversing with fellow patients but always in the same rhythmic style and always prolonging the first syllable after each intake of breath. After about a week of continuous practice in the clinic the patient is tested for speed and style. When the patient is fully at ease with his fellow patients and gains a speed of about fifty words, he is invited to partake in the debates held in the clinic every day. Whether the participants read out previously prepared speeches, or recite their pieces by heart or speak ex-tempore, the rules of speech are rigidly followed.

For about the first two weeks of treatment the patient is not allowed to speak to anybody outside the clinic. Since the clinic has no hostel accommodation, strict silence is enjoined on the patients after leaving the clinic and before coming back the next morning. The one reason that can be adduced in support of this rule would be that outside the clinic the patient would naturally fight shy of the new style of speaking and might relapse into the normal style with the inevitable relapse of the trouble. In my opinion what is of greater benefit in the Rami method of treatment is not the reading or supervised conversations and dialogues, but the fact that all the patients seem to forget the "unusualness" of the new mode of speech, which would sound very amusing to the outsider. In the earlier stages *i.e.*, until the patient regains full mastery over the entire chain of expressions (consonants, compound consonants, vowels, exclamations etc.) the speech of the patient under treatment sounds mechanical, monotonous and from the point of pronunciation, sometimes absolutely wrong. For instance, to say "Doctor, may I go to drink a cup of tea ?", the patient is made to say, "D-o-o-o-ctor, m-a-a-ay I go-o-o-o to dr-e-e-e-nk a c-u-u-up of t-e-e-ea ?" While a non-stammerer would not much notice the elongation of words like "Doctor," "may," "go," and "tea," the drawing out of the vowels in "drink" and "cup" would raise a smile, which would naturally make the patient more self-conscious and avoid the clinic style in private conversations.

During the group practice in articulation, *viz.*, during debates, narrations, platform reading, etc. the patients gain not only a practice in the new style of speech, but get rid of the deep self-consciousness and nervousness which are invariably associated with stammerers. Volunteer patients are allowed to take part in these group practices even if they have finished only three days of treatment. All the languages known to each patient are used for individual and group practices and conversation, so that stammerers who are bad in any particular language are given a chance of overcoming their individual defects in all languages known to them. In order to encourage the patients to speak out in front of strangers, outsiders are sometimes invited to watch the debate meetings.

When the Director felt satisfied that an individual patient had regained a rhythmic mode of speech without stuttering or stammering even once from the commencement of the treatment and when the patient had attained about 80 words' speed, he was taken out of the clinic by Mr. Rami for practice with strangers who did not know the patient or know that he was under treatment. He was encouraged to create short conversations with total strangers by inquiring for the prices of various commodities at various shop-fronts, by telephoning to strangers on some pretext or other, by buying tickets at cinema or railway stalls, by asking for time from wayfarers, by seeking directions from traffic policemen etc. All such essays into conversation with strangers were personally supervised by Mr. Rami himself or by an advanced patient detailed by him. This "outside" practice commenced with tackling about 15 strangers on the first day, and progressively fifty to seventyfive strangers per day subsequently. Before being declared to be completely cured, each patient will thus have spoken to about 500 to 750 strangers.

Since the incidence of stammer is the greatest under the stress of physical stress or exhaustion or excitement, the patient gets a further trial of speaking under these handicaps after about three weeks from the commencement of treatment. The patient for instance is confronted by a sudden but pre-arranged outburst of fury from the doctor or another patient, by sudden questions after a good stretch of running, an unwarranted discussion about the taxi-metre hire with the cab-man, a deliberately planned minor accident like a surprise tilting of the patient's chair from behind, etc. Until and unless the patient is able to handle all such unexpected situations in the rhythmic mode of talk, he is not declared to be free from stammer.

CASE REPORTS.—Being very much interested in Mr. Rami's method I had followed several cases at his clinic, of which the following are a few representative histories :

1. R. L., aged 22, Punjabi Hindu.

History:—The trouble started when the boy was about 6 years old, soon after tonsillectomy. About this time, he was very much in the company of a cousin who was a very bad stammerer. So that in this case, in addition to the shock of the operation, there may also have been present an element of mimicry. He was seen by me on 29–6–'52. At that time my findings were as follows:

General appearance: healthy. Weight 130 lb. Pulse 80. Temperature 98·4°F. Throat, lips, mouth, tongue: normal. Heart and lungs: normal. The nervous system was thoroughly investigated to rule out organic disease as cause of the trouble, and the findings were:

(1) Intelligence normal. (2) Speech: case of pure stammering. Stammers at the beginning of a sentence or phrase. Stammers less with strangers, and more with people he has a respect for: father, elderly friends of the family, girls etc. Gets exhausted after a short conversation on account of undue expenditure of breath. Stammers more in Hindi and Punjabi than in English. Reading speed about 90 to 100 words per minute. (3) No sign of organic disease was detected.

The device was fitted on the 30th of June '52 and the patient was taught to breathe with the device on: He was taught to read, and speak observing the following rules: (*a*) Lengthen the first syllable after intake of breath and break off at the third or fourth syllable as the case may be; (*b*) speak slowly, smoothly but firmly, practise the lengthening of the first syllable of a word or group of words for a long time every day.

12th July 1952:—I saw the patient again this day. His speed in reading was 50 sounds or syllables a minute and he did not have to make any effort of the facial muscles to articulate nor get exhausted. In the first 9 days of the treatment he was able to talk at 30 syllables per minute, then from the 10th to 18th day, 50 syllables per minute, 18th to 24th day, 70 syllables. His general health was very much improved and he was apparently getting over the inferiority complex which is so common in these patients.

18th July 1952:—The speed on this day was 75 syllables a minute.

9th August 1952:—The speed was 100 syllables a minute. He talked quite freely and was quite satisfied. He was made to speak very fast for a test at 150 to 200 syllables per minute. He did not stammer even once. For the next few days he was made to go for walks accompanied by Mr. Rami. On the way they spoke to at least a hundred strangers, and as he did not stammer at all, he was considered cured. The people he was made to talk to, were shopkeepers, pedestrians, ladies in the bus-queues etc. He was also made to speak to a number of people on the telephone.

He went back to Delhi towards the middle of August. His subsequent letters show that his people are quite satisfied with the results of treatment and the normal speech which he has now acquired continues unimpaired.

CASE II.—V. C., aged 31. Weight 98 lbs. Complained of stuttering, stammering and lisping.

History:—The trouble started when the patient was 5 years old. Gives no history of any disease or operation as the immediate precursor of the trouble. Says he had no opportunity for mimicry. The condition is progressive. He stammers more with strangers and elders or superiors. He can sing quite well and without difficulty. Does not give a history of any remissions as are seen in many cases. Stammers at almost every word. General appearance on 30-6-'52: rather on the thin side, temperature 97°F. Pulse 80%. Throat and mouth, eyes and tongue: normal. Heart and lungs: normal. The nervous system was thoroughly investigated to make sure no organic disease, as cause of the trouble, was present. The findings were: (1) Intelligence: normal. (2) Speech: stuttering, stammering and lisping present. Had difficulty in uttering every word, moved the head spasmodically whilst talking. The condition was progressive without any remissions at all. Very much worried over his handicap—as a result had developed an inferiority complex. (3) No sign of organic disease was detected.

The device was fitted on the 1st of July 1952, and he was taught to speak as detailed under Case 1.

12-7-'52:—Speed 40 to 45 syllables a minute. Could read smoothly, speak smoothly also. Speech rhythmical. Took breath regularly and evenly after every 4 syllables. Seemed happier, not self-conscious of his new mode of speech, and appeared to have adopted this mode even when talking to total strangers. Much improved in health, and felt that he would get over his impediments.

20-7-'52:–Speed 70 syllables a minute. Improvement continued. No hesitation. In the first week he was made to speak 30 syllables a minute, 50 during the second week, 70 during the third week and 100 during the 4th week. He was told that the last speed had to be maintained for at least 6 months.

9-8-'52:—Fifth week: Speed 100 syllables per minute. From the 12th onwards *i.e.* at the end of the 6th week, he was taken round to speak to perfect strangers and he came out of the test with flying colours, and left the clinic, as another of the many completely cured and happy patients.

CASE III.—R. M., aged 22 years:—*History*:—Started quite early in life. Seems to have imitated a servant girl in the house, who used to stammer. There is a cousin who stammers. No history of any fright, or operation or organic disease that may have initiated the trouble.

Examination:—Pulse 86. Temperature 98·4°F. Weight 125 lbs. Height 5'4½". Lips, mouth throat: normal. Heart and lungs: normal. Chronic discharge from the left ear accompanied by deafness.

The findings were:—(1) Intelligence: normal. (2) Speech: Case of pure stammering. Stammers so badly that his speed was hardly 40 words per minute. Stammered irrespective of who was present. Did not stammer when alone. No remissions. Took very long to get started on a sentence. Painful rigidity about the lips and the facial muscles during attempts to articulate. (3) No sign of organic disease was detected.

The patient was first seen on the 14th of July '52, and the next day the device was put on. I saw him again on the 26th of July *i.e.*, the 12th day of treatment, and found him very much improved. His speech was now 52 syllables a minute. The first syllable came out immediately without any effort. I saw him again on the 9th of August, the 27th day of treatment and found he had retrogressed. This was because he was self-conscious, and would not continue the mode of speech described above, which was taught to him, after leaving the clinic every day. This brings us to one hanidcap under which the Rami Clinic works, *viz.*, lack of facilities for residential accommodation during the period of treatment. The particular patient described in this case report was ostensibly ashamed or shy of speaking before his usual associates outside the clinic in the peculiarly drawn-out style. I saw him after some months of treatment *i.e.* some time in November 1952 and found a great deal of improvement which however, might have accrued earlier if he had been more co-operative or if, he could have been counselled to adopt the system in residential surroundings more congenial to his natural self-consciousness.

CASE IV.—C. K., aged 16. This was a case of very bad lisping without being complicated by stammering or stuttering symptoms. He was first seen on 5th July '52. Temperature 98·0°F. Pulse 90. Weight 108 lbs. Heart and lungs: normal. Lips, throat, palate teeth, tongue: normal.

History:—He had delayed milestones as a child and used to lisp from the very start. The father has a squint as a result of fright at his own shadow when he was a child of three.

The findings were:—He was inclined to be exceedingly nervous. (1) Intelligence: normal. (2) Speech: Nearly 23 letters of the English alphabet were defectively pronounced, so much so that not a single sentence in a reading demonstration of 15 minutes was intelligible. Some of his typical mispronunciations were the following: thuth (church), lun (run), thime (time), ethleet (streets), mole (more), peth (fetched), thath (dad), aye (hay), ath (has), Lam (Ram), etc. Since the Nagari alphabet is a more representative and scientific one, he was asked to read out the consonants in Nagari. Out of the 39 primary consonants he could pronounce

only 7 correctly, which he also used for the remaining 32. Finally he pronounced his own name Chandru as "Thandhlu". (3) No sign of organic disease.

I saw the patient again on the 26th July *i.e*, 21st day of treatment. I found him speaking much better He seemed to have got over every one of the defects. His health was better and his look less of a neurotic type. The nervousness which was initially very marked, seemed to have passed away completely.

Mr. Rami had to take much more pains with this case, and the period of treatment was longer. But eventually the patient left the clinic completely cured of every defect of lisping. He could pronounce even compound consonants clearly, though slowly. In this case also, the cure was effected on the basis of breath-control and practice, but without the aid of the palate device.

Biographical note on Mr. M. S. Rami:—It is deeply regretted that Mr. M. S. Rami whose method of Stammer Therapy has been detailed above died suddenly in Bombay on the 20th of April 1953.

Mr. M. S. Rami was born at Patan (Gujerat) about 44 years ago. At the age of eight he developed a slight stammer as a result of an accidental fall. The trouble was accentuated and confirmed within three years owing to his having been segregated in the class-room.

At the age of twenty-three, after having undergone all the systems of therapy commonly adopted in this country, *viz.* speaking with pebbles in the mouth, standing in neck-deep water and shouting etc., he lost all hopes of ever regaining normal speech. He left for Japan in order to learn Dentistry (he held a Diploma from Tokyo and thus came to be known as Dr. Rami), and while moulding dentures for his patients conceived the theory which was destined to be the genesis of his sensational method of curing stammerers: he thought that if a method could be found to control the intake and expenditure of breath of a stammerer artificially, the trouble could be solved. He invented a palate device for himself and practised laboriously at controlled respiration and articulation. Without any precedent for this method and without anyone's guidance he attained such a measure of success in curing himself that on his return to India he undertook the treatment of stammer cases in Nagpur, Ahmedabad and Bombay. The records at his clinic show a success in almost all of the hundreds of cases undertaken by him, with the exception of those whose speech defects were caused by organic malformation or damage.

Still what impressed one most was not so much the measure of success achieved by him as the amount of labour and sympathy he devoted to each individual case: patients were being accepted by him with due regard to their paying capacities, very poor ones being treated entirely free.

Though unfortunately his premature death removes from the Indian field the only recognized authority in handling speech defects successfully, the method of therapy perfected by him is still in use at the Rami Clinic in Bombay.

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SOME PHYSIOLOGICALLY ACTIVE NATURAL ORGANIC PIGMENTS*

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PART I

Flavonoid Compounds *vis-a-vis* Their Chemistry and Characterisation

Introduction.—Of the naturally occurring organic colouring matters, flavonoid pigments (derived from 2 phenyl-benzo-γ-pyrone structure) form an important group, some of which are characterised by their specific physiological properties. These colouring matters are found almost exclusively in plant materials and they occur in many parts of plants. The remarkably favourable results shown by some flavone derivatives upon the resistance and permeability of the capillary wall in certain pathological conditions seem to suggest that this large group of vegetable colouring matters also play a significant role in animal life and that they are of importance as vitamins as well. It is intended to set out in the following paragraphs a brief description of the more important members of this family of pigments with special reference to their chemistry and characterisation.

Flavonoid compounds *vis-a-vis* their vitaminoid activity.—Among the large variety of flavonoid series, citrin, rutin, gossypetin, quercitroside, rutoside and naringoside are examples of compounds found to exhibit pronounced physiological activity akin to vitamin P. Some salient aspects of these compounds are given below:—

1. *Citrin*:—This was isolated as the crystalline flavone glycoside fraction from paprika extracts and lemon juice, by Szent-Gyorgyi and co-workers (*Nature*, 1936, *138*, 27; *Deut. Med. Wochschr*, 1936, 62, 1326; *Nature*, 1936, *138*, 798) and was termed 'citrin' (citrus flavone) to indicate its chemistry, and also 'vitamin P' to indicate its vitamin-like effect on tissue-permeability. Chemical studies (Bruckner and Szent-Gyorgyi, *Nature*, 1936, *138*, 1057; Lajos and Gerendas, *Biochem. Z*, 1937, *291*, 229; *Biochem. J.*, 1937, *31*, 915) of citrin showed that it is a mixture of glycosides of previously known flavonone derivatives *viz.*, hesperitin and eriodictyol.

The glycoside hesperidine is a methyl derivative of eriodictine. Hesperidine forms the major part of citrin. The pronounced reactivity and the colour reactions of citrin are considered by Szent-Gyorgyi (*Nature*, 1936, *138*, 1057) to be attributable to the eriodictyol glycoside. However citrin contains no free eriodictyol. This substance could be isolated only after complete hydrolysis. As referred to above, eriodictyol is but a demethylated hesperidine. This leads to the assumption that both glycosides constituting

* Specially contributed to THE ANTISEPTIC.

citrin are but two forms of the same flavonone glycoside. Further, eriodictyol glycoside was not found in any considerable quantity in unripe oranges, which, at the same time, contain appreciable quantities of hesperidine. It is, therefore, surmised in earlier investigations that the eriodictyol glycoside is formed from hesperidine by demethylation on ripening of the fruit.

Subsequently, Mager (*Ztschr. f. physiol. Chem.*, 1942, *274*, 109) isolated an yellow, crystalline, water-soluble compound from citrin which was identified as eriodictyol rhamnoside. Scarborough (*Edinburgh M.J.*, 1944, *51*, 381) compared the activity of pure hesperidine with that of an extract from rose hips and concluded that hesperidine was not the most potent source of vitamin P activity and, therefore, could not be identical with the vitamin.

As early as 1938, Higby (*J. Am. Pharm. A. Scient.*, Ed. 1943, *32*, 74) studied a number of relatively crude flavone preparations from citrus peel including crude orange hesperidine, lemon citrin, calcium eriodictate from oranges and lemons, and lemon eriodictine. Orange derivatives, which contained no eriodictyol, were at least as potent as the lemon preparations which contained considerable quantities of this substance. These results therefore, led to the inevitable conclusion that an eriodictyol glycoside could not be the source of vitamin P activity. Further pharmacological tests with these crude preparations revealed the following results :—

(*a*) Pure hesperidine (administered as a suspension of crystalline needles in physiological saline solution), pure limonine (obtained from lemon peel), and pure eriodictyol had no activity.

(*b*) On the other hand, the water-soluble yellow pigment from crude orange hesperidine was found to be active. This was identified as hesperidine chalkone.

It was therefore concluded by Higby that insoluble, inactive, pure hesperidine was activated merely by solubilization and that its apparent low potency was only due to poor absorption. Wawra and Webb also reported (*Science*, 1942, *96*, 302) the isolation of biologically active hesperidine chalkone from lemon peel. The chalkone is considered to be capable of reversible oxidation and reduction as shown below :—

$$\text{Hesperidine chalkone (yellow)} \underset{\leftarrow OH}{\overset{\rightarrow H}{\rightleftharpoons}} \text{Hesperidine (white)}$$

It will be appreciated that the chalkones as a class are typically unstable, since they are formed from their flavonones by the action of mild alkali and revert readily in acid solution, or when heated. This is consistent with the "Biogenesis" theory advanced by Robinson (*Nature*, 1936, *137*, 172 ; *Phil. Trans. Roy. Soc.*, 1939, *230B*, 149) and later workers. Viewed in this light, hesperidine chalkone was considered by Higby to be no exception, since it reverted promptly to hesperidine on heating or even on long storage in the dry

state. This reversion can be prevented by causing the compound to be permanently water-soluble in the desirable pH range. This is achieved by stabilisation of the chalkone by controlled methylation of one of the hydroxy groups (at 6'-position), thereby converting it into hesperidine methyl chalkone. It is reported to possess a relatively higher vitamin P activity than that of pure hesperidine.

From the comparative results obtained on testing hesperidine, an impure sample of demethyl-hesperidine (mother liquor of 'citrin') and quercitrine for vitamin P activity, Szent-Gyorgyi and coworkers (*Nature*, 1937, *139*, 326) concluded that there is a great difference in the activity of different phenyl-benzo-γ-pyrones. Since the only essential difference in the formula of quercitrine and hesperidine is found on the C^2 and C^3 atoms, it is considered that these atoms are of special importance for the activity. Changing the flavonone hesperidine into the corresponding flavonol entails inactivation.

Synthesis of hesperidine.—Geza Zemplen and Rezso Bognar (*Ber.*, 1943, *76B*, 773-775) reported the synthesis of hesperidine by an interesting method. Following the discovery connected with the condensation of phloracetophenone glycoside with *p*-HOC_6H_4CHO to the corresponding chalkone, thus making possible the synthesis of *p*-phlorizin, an analogous synthesis of hesperidine was undertaken. Since hesperidine was known to be a β-7-rutinoside of hesperitin, the latter was the starting compound for the synthesis. Hesperitin and acetobromorutinose were finely powdered together and thoroughly kneaded with freshly distilled quinoline. The mixture was treated with active silver oxide, stirred and allowed to stand for a few hours in a sulphuric acid desiccator. The contents were then diluted with acetic acid with cooling, centrifuged from the silver compounds and poured into water. The resultant smeary precipitate was dried, and repeatedly treated with chloroform and alcohol. It was finally taken up in alkali and regenerated by addition of acid.

Recently, Scarborough (*Biochem. J.*, 1945, *39*, 271) has drawn attention to the probable multiple nature of vitamin P. It is considered by him that the activity of pure hesperidine is not sufficient to account for the potency of many plant extracts. It is suggested that the active material might consist of a group of flavonones.

2. *Rutin*:—This was discovered by Weiss (*Chem. Zentr.*, 1842, 305) in the leaves of rue (*Ruta graveolens*, Linn.). Zemplen and Gerecs (*Ber.*, 1935, *68B*, 1318) found that rutin, a rhamnoglycoside of quercetin available in tobacco possesses pronounced physiological activity in increasing capillary resistance in man (Griffith *et al*, *Proc. Soc. Exptal. Biol. Med.*, 1944, *55*, 228). Couch, Naghski and Krewson (*Science*, 1946, *103*, 197) found that buckwheat (*Fagopyrum esculentum*) is a promising source of rutin.

Pollard (*Nature*, 1942, *150*, 490) obtained a very active anthoxanthin glycoside preparation from black currants.

The chemistry and characterisation of rutin are very interesting. Zwenger and Dronke (*Ann. Chem. Pharm.*, *123*, 145) showed that it was not identical with quercitrin but differed from it in that it gave on hydrolysis one molecule of quercetin and two molecules of sugar. Schmidt (*Chem. Zentr.*, 1901, *ii*, 121) pointed out that of the two molecules of sugar one was glucose and the other rhamnose. Rutin was assigned the formula $C_{27}H_{30}O_{16}$. It is now known that the sugar is a biose, termed rutinose.

Attree and Perkin first investigated the position of the sugar residue in rutin, On methylation with diazomethane, the above workers obtained a yellowish orange resinous mass. This was hydrolysed with 7% sulphuric acid and the resulting product compared with 3-hydroxy-5:7:3':4'—tetra-methoxy flavone (Kostanecki and Tambor, *Ber.*, 1904, *37*, 1402). They were identical. Hence it was concluded that rutin is a 3-glycoside. The concerned 3-hydroxy compound does not undergo degradation smoothly and was originally synthesised by the method of Kostanecki (*Ber.*, 1904, *37*, 1402) involving several steps. Recent work (Seshadri and coworkers, *Proc. Ind. Acad. Sci. A.*, 1949, *29*, 80) has shown that its ethyl ether suffers smooth fission and this mixed ether as well as its fission ketone can be synthesised readily and could therefore serve as reference compounds in further investigations in this series.

3. *Gossypetin*: —As early as in 1899, gossypetin was isolated by Perkin (*Chem. Soc. Trans.*, 1899, *75*, 826) and has been completely studied (*ibid.*, 1913, *103*, 650). A full account of this compound is contained in "The Naturally Occurring Organic Colouring Matters" by Perkin and Everest, 1918, page 224. Clark and Geissman (*Nature*, 1949, *163*, 36) found recently that gossypetin possesses high vitamin P activity (16 times that of rutin on a weight basis). Activity in respect of this compound was assessed on the basis of its ability to increase the duration of the relaxation of the isolated mammalian intestinal segment by epinephrine in the presence of cupric ion (this being one of the vitamin P characteristic).

4. *Quercitroside.* 5. *Rutoside.* 6. *Naringoside* are also found to be capable of maintaining in the test organism a certain circulating concentration of sympathin and thereby arresting the auto-oxidation of adrenaline—an activity similar to that of vitamin P. (Lavollay and Neumann, *Compt. rend.*, 1941, *212*, 251–253; *Chem. Zentr.*, 1942, *1*, 1395).

Conclusion.—It will at once be evident from the foregoing that certain anthoxanthin compounds possessing a flavonoid structure are capable of exerting vitamin P-like action in the system and thus seem to have an important biological role to play.

ISONICOTINIC ACID HYDRAZIDE*

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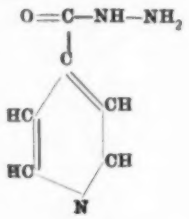
ISONICOTINIC acid hydrazide was synthesised in the year 1912, but its value in tuberculosis was discovered recently by the research workers of Messrs Squibb and M. Roche.

Properties and actions.—It has the following structural formula.



It is colourless and soluble in water.

In vitro.—INAH is tuberculostatic and tuberculocidal. Presence of serum in media slightly affects the activity of the drug.

In vivo —Guinea pigs infected with virulent human tubercle bacilli and then treated with INAH did not show appreciable evidence of tuberculosis. No evidence of bactericidal action in human-beings is reported.

Absorption, distribution and excretion.—When given orally, it is rapidly absorbed from the gastro-intestinal tract. Maximum plasma concentration is obtained within 1 to 6 hours. It gets evenly distributed in all the tissues and body fluids. It is present in the cerebrospinal fluid and the fluid of pleural effusion. Most of the INAH absorbed, is excreted by the kidneys, within 24 hours; no cumulative toxic effects are therefore, likely to be produced.

Therapeutic effects.—It was prematurely announced in the press that INAH is a wonder drug which would cure tuberculosis and which would work miracles and revolutionise the treatment of tuberculosis. It has however since been found that such a report had raised great but false hopes in thousands of patients suffering from tuberculosis. The results obtained by treating patients with INAH have not been in anyway better than those obtained with streptomycin and PAS.

When INAH is given to patients suffering from tuberculosis, the temperature comes down within 2 to 3 weeks. The cough and the amount of sputum decrease, also the number of tubercle bacilli in the sputum. The sputum may even become negative on microscopical and cultural examinations. The patient develops a sense of well-being. The appetite increases and the patient

* Specially contributed to THE ANTISEPTIC.

puts on weight. The X-ray picture shows improvement, which is not commensurate however, with the improvement in the general condition. The erythrocyte sedimentation rate shows wide variations. I have observed that the sedimentation rate of patients treated with streptomycin, PAS and INAH is much lower—practically normal—than that of those cases who are treated with streptomycin and PAS.

As INAH diffuses in all body-fluids, it is useful in treating T.B. meningitis. It readily combines with intra-muscular streptomycin, and therefore, there may not be any necessity for giving streptomycin intrathecally.

Dosage :—3 to 5 mg. per kg. of body weight per day. (150–300 mg. per day for an adult). Larger doses up to 10 mg. per kg. of body weight have been given to those suffering from T.B. meningitis without any toxic effects. It has not yet been determined as to how long INAH should and could be continued.

Toxic effects :—Recent reports show that there are no serious toxic effects when it is given for only a short time. We still do not know the after-effects it may produce, on prolonged use. The following toxic effects have been reported so far :—

Constipation, difficulty in starting micturition, restlessness, insomnia, exaggerated reflexes, postural hypotension, albuminuria, eosinophilia, slight lowering of hæmoglobin.

Drug resistance.—This is indeed a serious factor which limits the usefulness of drugs against tuberculosis ; when given alone, tubercle bacilli develop resistance within a relatively short time. In one case drug resistance developed as early as the 26th day of treatment. Drug resistant strains were isolated, after three months of treatment, from 70% of cases whose sputum remained positive. It is advisable to combine INAH with streptomycin or PAS.—preferably with both, to prevent such drug resistance which is indeed a serious factor to reckon with.

(Continued on page 596).

Eosinophils in Peripheral Blood of Typhoid Patients

Mazzolini made eosinophil counts by the thick drop method in 64 patients with typhoid. In 12 the eosinophil curve was followed during the entire course of the disease. Leucopænia was present in 87% of the patients (average of 3000 leucocytes per cm.m.). It was not however, charactoristic of any particular phase of the disease. Eosinopænia was found in 92% of the patients, in 27% of whom the eosinophils had disappeared from the peripheral blood. This may become *an important factor in the diagnosis of typhoid*. Eosinopænia was a marked early and constant phenomenon and was present in the first phase of the disease when serum diagnosis was not as yet positive. It persisted during the second phase and began to disappear in the third phase, when clinical signs indicated subsidence of the disease. Thus, their *reappearance in the peripheral blood* may become one of the *first signs of recovery* from typhoid. However, this does not justify in interruption of antibacterial (especially chloramphenicol) therapy. From his experience, Mazzolini advises continuation of therapy in gradually decreasing doses for 12 to 15 days thereafter.—(Abst in *J. A. M. A.* 150. 2. p 252 from *Sett Med* 40. p 156)

A note of caution.—INAH is an useful weapon against tuberculosis, but it should not be used indiscriminately or haphazardly. If used improperly, not only would it decrease the chances of the patient benefiting by other forms of therapy, but drug resistant strains might develop which would infect other individuals. During treatment frequent urine examinations, blood counts and neurological examinations must be done. It should not be used as the sole treatment for tuberculosis but only as an adjunct to the time-honoured measures of bed-rest, collapse therapy, surgery and nutritious diet.

References:

1. Year Book of Medicine, 1952. 2. Modern Treatment Year Book, 1953.

Caution in Treatment of Renal Tuberculosis with Isonicotinic Acid Hydrazide (INAH)

When kidney excretion is impaired this drug may accumulate in the blood of the uræmic patient causing serious convulsions. Muscle twitching, spasms and liver damage also may be caused by retention of the drug. Though it is effective in kidney tuberculosis and improves bladder lesions, the precaution of making blood tests to determine retention is necessary. This new drug presents limitations when *not* used in conjunction with Streptomycin and PAS. The presence of large amounts of necrotic tissue in massive kidney lesions renders the drug ineffectual in sterilizing the urine and resistance to the drug may be developed by the tubercle bacilli in 2 to 8 weeks. The combination of Streptomycin, PAS and isonicotinic acid hydrazide may however greatly increase their effectiveness and further defer the development of drug resistance. Modern chemotherapy may modify the tethal course of renal tuberculosis.—(*Internal. Med. Abst. and Rev.*, June 1953 from *J.A.M.A.*).

INAH in Miliary and Meningeal Tuberculosis

Clark *et al* treated 25 patients with miliary and meningeal tuberculosis : 10 had miliary tuberculosis, 4 had miliary tuberculosis complicated by meningitis and 6 had meningitis alone. Five cases with meningitis received streptomycin in addition to INAH. All patients received approximately 10 mg. of INAH per kg. of body weight daily during the first week, then the dose was reduced to 7½ mg. Two of the 10 patients with miliary tuberculosis died within 4 to 6 days after starting the treatment. There was remission in all other cases of the infection. In the six cases of meningitis treated with INAH alone, abnormalities present in CSF at the start receded and normal values reached by 22nd week—in five out of the six cases.—(*Med. Rev. Rev.*, June 1953 from *Am. Pract.*, March 1953).

INAH and Carbohydrate Metabolism

Luntz and Smith report that an average daily dose of 312·5 to 334 mg. of INAH was given to healthy persons and diabetics. The plasma level of INAH varied from 0·41 to 0·5 mg. INAH produces a temporary elevation of blood sugar level. The insulin requirements of diabetics receiving INAH may be increased.—(*Med. Rev. Rev.*, June '53 from *B.M.J.*, 7-2-'53)

A CASE OF FACIAL PARALYSIS WITH MORALS

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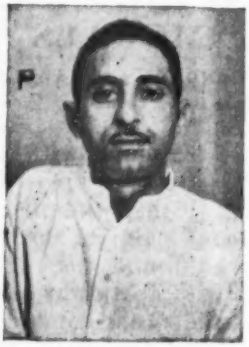
MR. B., aged 28 years, started his illness with acute otitis media and otorrhœa in June '52. He was treated by an ear-nose-throat specialist in Bombay till 18th September '52, when he was seized with a severe otalgia and pain in the right mastoid area. On the morning of the 20th, he found his right eyelid and lips heavy, which developed into a complete right side facial paralysis, during the course of the day. He was treated by the ear-nose-throat specialist, who administered penicillin and aneurine injections till the 24th, when he came under my care.

C.O.E. : His main complaint was ear-ache. Auroscopic examination revealed a throbbing tympanic membrane of the right side and X-ray showed right mastoid sclerotic. Left mastoid was pneumatic. Rinne's test was negative on the right side and Weber's test positive *i.e.*, best heard on the left side. There was loss of taste on the right side of the tongue, showing involvement of the chordæ tympanic nerve, as well. It was decided to do a conservative mastoid operation. This was performed on the 28th September. The right mastoid was found sclerotic. Cells were opened up and cleaned. The facial canal was not opened and the nerve not decompressed. The surgeon after cleaning, closed the mastoid in the usual way with the drainage tube. The patient developed serous labyrinthitis with intense vertigo on the 30th September, which responded to aureomycin, 500 mg. *stat* 250 mg. every six hours for 3 days. On the 12th Oct., he was put on diathermy and on the 20th Oct., it became possible to provide electrical treatment. The preliminary reactions before starting the treatment showed Erb's reaction of degeneration with loss of faradic response. This electrical treatment consisted of interrupted galvanic current (Karamchandani, 1953). It was given for 10 minutes every alternate day till the 17th December. The first set of photographs was taken on the 11th November '52. Various movements are annotated in the legend (*vide series 'A' on page 598*). On the 18th December, the faradic response returned, while the galvanic response showed (1) Kcc> Acc>, Aoc> Koc (2) Minimum current for response 2 m. amps./sec. Electrical treatment was temporarily stopped now with a view to preventing contractures from developing and for watching further progress. Further, the machine went out of order and the patient left for home. The second set of photographs taken on the 27th December '52 shows great improvement (*vide series 'B' on page 599*). In addition to the electrical

treatment, he was given massage and controlled exercises and other treatments (*vide* THE ANTISEPTIC, Feb. 1953, p. 86).

The patient returned from home on the 10th Feb. '53 and presented himself for examination, when his four-posture photograph was taken, (*vide series C and the legend on page 600*). There has been improvement in so far as, no distortion of any kind is visible on rest; but a slight cosmetic defect is noticeable on whistling and smiling. The patient is however, quite pleased and has resumed normal activities including going to the pictures. I don't recommend further electrical treatment because continuance may result in contractures and deformities. As a matter of fact, the machine went out of order at the right time in this case.



A—Face at rest—7½ weeks after complete right facial palsy. Drooping present.

A1—Face on showing teeth. Considerable drooping.

A2—Face on pursing lips. Drooping apparent.

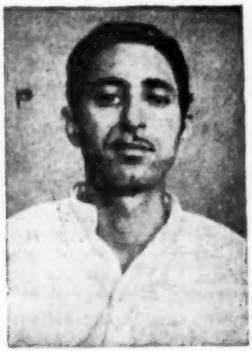
A-3—Face on closing eyes tightly. Complete right side palsy.

11-11-'52.

(Side of Palsy is indicated by 'P' in the photographs).

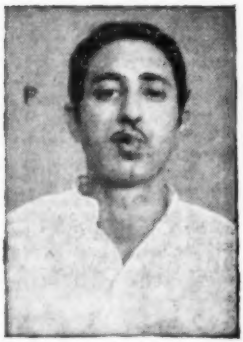
I have another lady patient variety 4*b*, whose photographs I should have liked to give for comparison. She did not take electrical treatment but received all imaginable therapies from specialists and consultants of Bombay city. The results were very poor. There is distortion even at rest. Unfortunately her photographs cannot be made available. Hers is a sad case.

In my experience, correct electrical treatment along with heat, exercise and massage has yielded the best results. The above male patient had been declared incurable elsewhere, where he had gone after the operation and before the commencement of the electrical treatment.



B—Face at rest—14 weeks after onset of palsy and 9 weeks after electrical treatment *vide* case notes. Almost normal face—no drooping.

B-1—Face on showing teeth. No drooping. Better preformance.



B-2—Face on pursing lips. No drooping, no associated movements of winking.

B-3—Face on closing eyes tightly. Noticeable extent of recovery.

27-12-'52.

(Side of Palsy is indicated by 'P' in the photographs).

Discussion.—This case raises certain questions to which I have furnished answers.

1. *Q.*—What is the prognosis in such cases ?

A.—Rather very bad. In fact, this case had been declared hopeless.

2. *Q.*—Should otitis media have been treated surgically ? And could facial paralysis have been averted ?

A.—Yes. Chronic otitis media is always a potentially erosive disease which can spread locally to VII N or inner ear or intra-cranially. The present case fell in the inaccessible group of Mc. Guck (1952). Surgery was indicated in order to ward off complication of facial paralysis.

3. *Q.*—If surgery was indicated, when should the surgeon have intervened and with what objective ?

A.—Acute otitis media commenced in June '52 and three months is the dividing line between development of the acute and chronic conditions. Therefore, to preserve function and ward off threat of dangerous complication, operation was indicated within three months. The objective was to provide safe hearing and a dry ear which can now be attained in 90% of the cases (James 1952). Livingstone (1952) has nicely summed up the situation as follows:—"In the mastoid group of otitis where the discharge is persistent and the hearing is affected, the guiding factor is the particular pathological lesion which must be removed entirely and the action must be to produce a safe hearing, and dry ear."

C—Face at rest—21 weeks after onset of palsy and 16 weeks after electrical treatment *vide* case notes. Normal face. No distortion.

C-1—Face on showing teeth. There is associated movement of right ocular muscles.

C-2—Face on whistling. He appears to wink. An example of mass move ment. A cosmetic defect *vide* Antiseptic, Feb. '53, p. 84.

C-3—Face on closing eyes. Right eye is completely closed though there is slight drawing up of right angle of mouth.

14-2-'53.

(Side of Palsy is indicated by 'P' in the photographs).

4. *Q.*—Is there any association between chronic otitis media and poorly pneumatised mastoid? In other words is the sclerosis a result of infection or of heredity.

A.—The present day concensus of opinion is that frustration of pneumatisation occurs when air is unable to circulate in the pneumatic system owing to:—

(*a*) Chronic nasal catarrh blocking the eustachian tube. (*b*) Minor non-suppurative attacks of otitis media, bringing about an osteitis, resulting in a dense mastoid. (*c*) The amazing frequency with which cellular mastoid on one side and acellular on the other is encountered, forces the conclusion, that the condition is acquired and not inherited.

Summary.—Details of a case of degeneration-paralysis of the facial nerve, variety 4*b* (*vide* The ANTISEPTIC, Feb. 1953, p. 83) are given below :—

Otitis media with otorrhœa. Commenced in June 1952.
Facial paralysis started on 20th September '52.
Conservative mastoid operation on 28th September '52.
Serous labyrinthitis developed on 30th September '52.
Discharged cured from the nursing home on 10th Oct. '52.
Diathermy commenced on 12th Oct. '52.
Electrical treatment commenced on 20th Oct. '52.
Electrical treatment discontinued on 17th Dec. '52.
Finally discharged on 14th Feb. '53.

Progress.—Paralysis commenced on the 20th Sept. '52 and electrical treatment on the 20th Oct. '52.

Pose A taken on 11-11-'52 shows complete paralysis.
Faradic and galvanic response normal on 18-12-'52.
Pose B taken on 27-12-'52 marked improvement.
Pose C taken on 14-12-'53 shows continued improvement.

Faradism was lost from 20-9-'52 to 18-12-'52 and galvanic excitability incomplete from 20-10-'52 onwards *i.e.* 5th week.

Therefore, this was a borderline case whose chances of recovery were 50/50 and the prognosis therefore, was not hopeless. Good results were promised with perseverance. *Sequlae and abnormal phenomena* :—Paralysis lasted from 20-9-'52 to 18-12-'52, Contracture significant; Spontaneous muscle contraction—nil; Reflex irritability—nil; Associated movements—present, slight; Gusto lachrymal reflex—present, slight; Auricular syndrome—nil.

Conclusion.—Patient received daily treatment, with diathermy, then interrupted a galvanic current, every alternate day for a litlte less than two months.

Results.—Recovery in five months, by degeneration. Disfiguring effect nil. Cosmetic results fair.

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2. James, J. A. (1952)—Lancet, II, 1207.
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TWO CASES OF HÆMATURIA

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CASE I.—U. N. K., Hindu, male, aged 20, District Barisal, East Bengal. Urine of this patient collected at about *11 a.m.* (marked as a case of hæmaturia) sent to my laboratory for examination by Dr. N.M. Mukherjee, revealed :—Colour reddish, reaction alkaline, albumen abundantly present; deposits with shreds of mucus. On standing the urine showed a tendency to coagulate. R.B.C. and W.B.C. abundant under microscope. Nothing else significant detected.

Next day, I saw the patient and took the history in detail which showed :—(1) A year and a half ago, one night he had a *sudden stoppage of his urinary flow.* He had a painful feeling of an obstruction at the root of the penis; after suffering for the whole night, he passed urine at about 9 a.m. on the next day. And he thinks that the urine was then clear.(?) (2) After being well for four or five months, he then *suffered at intervals* (more or less regular) till today from troubles like (*a*) difficulty and burning sensation during micturition—urine sometimes cloudy, red with blood or with "*some semi-solid substance floating,*" (*b*) pain in the lumbar region and constitutional symptoms like headache and fever.

I got him admitted into the hospital with the permission of the Superintendent. The blood examination showed eosinophilia of 20%. The examination of his blood taken at midnight was positive for microfilariæ. A specimen of his urine (*night collection*) on the next day was examined and along with other usual findings of previous occasions, living microfilariæ were found in fair number. There was however, no external filarial manifestation ; a local examination of his genitals revealed a faint scar on the right scrotum—post-operative to a hydrocele he had three years previously. No microfilariæ could be seen in specimens of urine collected during day time.

CASE II.—S.P. Hindu, male, aged 21, District Barisal, East Bengal.

Present history:—This patient had a sudden stoppage of the urinary flow early in the morning of a particular day about a month previously. He was relieved by cathterisation in the Ranaghat Hospital. Since then he had several such attacks with similar catheter-relief in the hospital. The urine from the very beginning had always been more or less mixed with blood, sometimes with some 'solid masses'. After having thus suffered for a month, he came for treatment to the Medical Officer, in-charge of the out patient department here in this camp. His urine was sent to me for necessary examination and report.

Urine:—red, alkaline, albumen abundantly present as also deposits; R.B.C and W.B.C. abundant. A few epithelial cells. Fat particles *nil*. No other abnormal findings to report.

When I contacted the patient on the next day, I could obtain no definite past history of complaints suggestive of filaria. He was admitted into the hospital. Leading questions, mainly in relation to the genito-urinary system elicited that about a year earlier he had a painful swelling in his right inguinal canal. It subsided so quickly that he took no notice of it and did not consider it sufficiently important to report when questioned previously.

Local examination:—Spermatic cord and epididymis of the right side comparatively thicker and very slightly tender. Testes and scrotal skin, penis and lymph glands—normal. Left side—no abnormality.

General examination:—Well-built. No apparent outward manifestation of filarial infection. *Blood*—Eosinophilia of 22%. Midnight blood—positive for microfilariæ. *Urine* (night collection)—same as that on previous occasion. No microfilariæ present. *Urine* (day collection) was also negative for microfilariæ. Repeated daily examinations of night and day collections of urine proved negative for microfilariæ.

Discussion.—1. History-taking is very important, particularly about the 'Periodicity' of complaints of a similar nature. In Case No. 1, the typical 'periodicity' of his complaints, suggested the possibility of a filarial infection. In Case No. 2, such a history was of course, lacking, because he took medical advice and treatment every time he had urinary trouble. Both the cases showed the presence of microfilariæ only in the midnight blood.

2. The *urine* in these cases varied so much that it would be a mistake to rely on the typical clinical characters, such as 'Chyluria'. or 'Hæmato-chyluria'. A tendency for the urine to coagulate on standing, indicates however that the urine should contain 'Chyle' or 'Lymph'. This was an important factor noticed in Case No. 1. The urine in some cases may contain only a small quantity of lymph as the abnormal element—when it is described as 'Lymphuria'. In neither of these 2 cases, was fat present in the urine, but lymph was present along with the other abnormal elements. Strictly speaking, the urine in these 2 cases might be described as 'Hæmato-lymphuria', though visually it was just hæmaturia'. Case No. 2. with the sudden onset of symptoms in youth might have led some doctors to think that it was probably a case of gonorrhœal infection.

'Retention of urine' without any previous warning as seen in both these cases obviously due to some lymphous coagula or mucous plug, has been described by some authors to be a common feature in the onset of the disease.

3. *Microfilariae in the urine*:—In Case No. 1, microfilariæ were present both in the urine and the midnight blood. While in Case No. 2, neither the night collection (8 p.m. to 8 a.m.) nor the day collection (8 a.m. to 8 p.m.) was positive though the midnight blood alone was positive. The infection in both cases was undoubtedly due to W. bancrofti (nocturna). The absence of microfilaria in both day and night specimens of the (urine in Case No. 2 was confirmed at successive daily examinations over a few days, though the urine was always blood stained in appearance. "The sanguineous appearance of such urine is due in some instances to the formation of blood-corpuscles in lymph long retained in the varicose vessels, as a result of the normal evolution of the formed elements in that fluid. In other instances, it is probably caused by a rupture of small blood-vessels into the dilated lymphatics". If the presence of blood in the urine of Case No. 2 be attributed to the first of the two explanations above, the absence of microfilaria in his urine is easily explained, as being due to some regional lymphatic obstruction, although the blood remained positive for microfilariæ all the time. Case No. 1 of course, comes under the second explanation (rupture of blood-vessels of the urinary channel, mainly of the bladder). That is why perhaps the first specimen of urine was not positive for microfilariæ.

4. Such cases are not at all uncommon, in India; the absence of any external manifestations of filarial complications is perhaps nothing abnormal too, as shown by these two cases. But the possible history of a hydrocele or of any inflammatory swelling of the cord, epididymis or testes preceding urinary troubles in filarial cases should not be lost sight of.

I am grateful to the Hospital authority and the Medical Officer, O.P.D., for their co-operation, in my investigation of the 2 cases.

Reference: Manson's Tropical Diseases, 1951.

Sodium Fluoride Therapy in Filariasis

Dr. R. Subramaniam, M.D., M.R.C.P., records successful results in 16 cases of filariasis by the use of sodium fluoride. The late Dr. Venkatachalam Pillai, Professor of Pharmacology in the Madras Medical College, made in 1945, a very interesting and important observation on the incidence of filariasis, that the condition was not to be seen at all in people residing in places where, fluorosis was *endemic*. He treated patients with filariasis by administering an one per cent solution of sodium fluoride, by mouth. Dr. Subramaniam treated the 16 patients by administering 1 c.c. of an one per cent solution of sodium fluoride, subcutaneously for 4 weeks at intervals of one week between two injections. He found the results to be uniformly good in all cases, and particularly successful in moderate-sized filarial legs.—(*Med. Rev. Rev.*, June 1953 and *J.I.M.A.*, June 1953, 151–155).

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THE SHORTENED M.B., B.S. COURSE FOR LICENTIATES

(DISCONTINUED BY THE MADRAS UNIVERSITY FROM APRIL 1953)

AFTER a long and strenuous struggle for over 25 years, both in the press and on platforms, the L.M.P. course was abolished from 1st April 1938, by the then Health Minister Dr. T. S. S. RAJAN, who took courage in both hands and straightaway ordered the discontinuance of that course which had been the cause of much bitterness among medical licentiates in India. At the same time provision was made by the Madras University for enabling the L.M.Ps. to take a shortened course and appear for the M.B. B.S. examination for obtaining a degree. Necessary rules were laid down for this purpose and a number of licentiates have since availed themselves of this condensed or shortened course. But the decision by the Madras University to discontinue this concession from April 1953 while a fair number of licentiates who took the L.M.P. course prior to 1938 are still waiting for no fault of theirs, to take advantage of the course is indeed, very unfortunate. They would have gladly taken the course and obtained their degrees during the 15 years that have elapsed since the abolition of the L.M.P. course in 1938, but for the fact that admissions to the course were so restricted as to make it difficult for many of the Madras licentiates to join the classes and readily benefit by the concession.

In the letters published elsewhere in this issue, Dr. D. V. VENKAPPA who has toiled long and hard for the uplift and amelioration of the lot of the licentiates in India, deplores this hasty and inopportune decision of the Madras University and has brought out certain facts which explain why all the licentiates of our State who desired and continue to desire to take the M.B., B.S.

degree have not been able to do so till now. The fault has not been theirs. We understand from Dr. VENKAPPA's well-argued and forceful appeal, that preferential treatment was given to certain licentiates *e.g.*, those in government and local board services, those with war service and some from other States, to the exclusion of the private practitioners in this State. He cites the case of a few licentiates in this State who have been unsuccessfully applying for admission continuously for a number of years. We are glad that Dr. VENKAPPA has left no stone unturned to help these unsuccessful disappointed licentiates out of their sense of frustration.

We are not however, told the reasons underlying the University's decision to discontinue the concession nor do we know how many more licentiates of this State still remain on the waiting list or to be brought thereon, who *really desire and will take* the condensed degree course. But it is our considered opinion that this concession which was granted in 1938 after mature deliberation by the University authorities for creating an uniform standard of medical education and medical practitioners in the State should be continued till all willing licentiates get absorbed into this uniform cadre with a single registrable qualification and we sincerely hope that our popular Vice-Chancellor who has all along been insistent on not lowering the standard of educational qualifications for medical practitioners as a whole, will reconsider the matter and make arrangements to continue the concession for the next three years till 1956, which is after all what is desired by the licentiates and by the Indian Medical Council. We note that the trend of public opinion in this regard as revealed in the medical and lay press of India is also distinctly in favour of such a procedure. We learn that an influential deputation of leading medical men has since waited on the State Health Minister and requested him to prevail upon the University authorities to continue the shortened course for 3 years more from 1954; and we earnestly hope that this modest request will not have fallen on deaf ears.

A SUCCESSFUL AND PROMISING VOLUNTARY SCHEME OF RURAL MEDICAL RELIEF

THE good work done by the medical students of four of the medical colleges in the State (The Madras Medical, Stanley, Vellore Mission and the Vizagapatam Medical Colleges) during recent months in villages not very far away from their respective colleges, is a fine example of the real good service rendered by students and of the excellent results obtained by voluntary effort in the direction of rural medical relief, given the requisite enthusiasm and will to serve, as also the cooperation of the local villagers. The students of the Stanley Medical College and the Vellore

Christian Mission Medical College have been engaged in rural uplift work for sometime now. The more recent addition to the ranks of these voluntary workers is the team from the Madras Medical College, which has been engaged silently during the last twelve months in carrying out health surveys and providing medical relief in a village named Pakkam 24 miles from the Madras City. Guided by the Dean and members of the College and General Hospital Staff thirty medical students and four doctors visit the village every Sunday carrying medical supplies and equipment in the hospital bus. On reaching the village a complete clinic is set up with counters for registration of cases and examination of men and women patients, minor surgery, injection etc.; a leprosy unit as also a dispensary unit are also laid out in a central place in the village, where the Women's Welfare Department is working already in an extensive compound. The whole idea behind this very useful humanitarian social service was inspired, so we are told, by the President of the Students' Association and the Dean of the Medical College acting in close cooperation.

On each visit this team attends on about 500 patients coming from different villages. During vacations, the students stay in the village, setting up a Health Survey Camp to assist in cleaning the village, improving the village sanitation by providing latrines, chlorimating wells, carrying out vaccinations and inoculations when necessary, giving talks with the help of cinema films on nutrition, child welfare etc. All such work which has been of immense benefit to the hitherto helpless rural population and which has necessarily resulted in savings to Government has been planned and executed by the students and teachers of *their own free will and accord* without even a suggestion from Government.

This laudable venture attracted the attention of the WHO Regional Officer at Delhi. Mr. Edwin Cameron, Adviser to the Regional Director wrote to the Dean of the College, "It is not only an interesting but a very practical way of providing medical relief and at the same time giving valuable experience to students in an aspect of medicine they very rarely see until after graduation, namely the patient in his own natural environment. The plan is so advanced not only for South East Asia but elsewhere that we would impose upon you further for additional information." The WHO Regional office sent a questionnaire to the Dean who, has since furnished details of the plan of work of the "*Rural wing of the Medical College Students' Association.*" The scheme we learn, originated primarily as a means to provide medical relief to villages and also serve the purpose of training students in the social aspects of medicine. Students of the 2nd, 3rd, 4th and final years of study participate in this noble work; the actual duties allotted to each naturally vary in onerousness and dexterity with the year of study. The most important and valuable part of this

scheme is that it does not cease to function at the close of the academic year but continues also into the summer vacation; the students resident in the city, without going to their homes for the vacation, continue to maintain the work. A Rural Health Survey Camp as part of the essential training for the students engaged in this work—was started with ten students on May the 17th 1953 and ended on the 7th of June 1953. The village comprises 8 hamlets with a total population of 5000 composed almost entirely of agriculturists and labourers. They had to travel many miles to Trivellore for medical relief till this scheme was put into operation. The Survey camp scheme for 3 weeks is estimated to have cost Rs. 1450 in all and the Dean is reported to have addressed the State Government for an allotment from the funds set apart by the Planning Commission. Each Sunday-afternoon-visit costs nearly Rs. 200 and the State government cannot be unmindful to the necessity for promptly sanctioning the necessary funds for carrying out this efficiently-working voluntary scheme which benefits thousands of villagers at a nominal cost to the State.

If such well-planned schemes are suitably aided by the State, there will be no dearth of volunteers for such humanitarian work without the necessity for any compulsion.

THE STATUS OF OUR PRESENT KNOWLEDGE RELATING TO THE METHONIUM COMPOUNDS

CONTROL of hypertension by the hitherto known and available measures has so far presented a difficult and baffling problem to the medical profession. Low sodium and restricted diets, psychotherapy, sympathectomy and the administration of many different drugs, have all yielded good results in some cases and failed in others.

Dr. ING. at Oxford had been experimenting with various compounds in relation to curare and along with Dr. BARLOW, prepared a series of bis-quarternary compounds which included the methonium series. Dr. PATON of the University College Hospital Medical School tested several di-basic compounds one of which was octa-methonium, to see if a change in the terminal grouping of such compounds would alter the property of histamine liberation. The pharmacological properties of a number of these compounds, were investigated by KING, ZAIMIS and PATON.

The most important outcome of all these researches was that when the chain was shortened, not only did the neuromuscular paralysing action almost disappear but a new action was revealed *viz.*, ganglionic block. Thus resulted two methonium compounds the deca- and hexa-methonium of high activity and considerable specificity of action, useful for clinical and scientific purposes.

Decamethonium.—At surgical operations, d-tubocurarine was being used to overcome the seriously interfering abdominal muscle-contractions that impeded the surgeon, sometimes seriously. It was not cheap and had certain undesirable side-reactions, due to the release of histamines; often it produced paralysis of the ganglia which contributed to a fall in the blood-pressure. Decamethonium was first tested on cats and then clinically in human anæsthesia and found to be a satisfactory muscle relaxant, possessing a shorter duration action than d-tubocurarine; the need for an antagonist is not really so very pressing, in view of this short duration.

Decamethonium was found very satisfactory in the treatment of tetanus and of spastic diseases also. Dr. KEIR found it to be very effective in a number of cases of tetanus treated by him with decamethonium iodide *(Br. Med. Jour.*, 2: 984–985, 1950). In spastic states on the other hand, like other muscle relaxants, "it did not prove possible to relieve the overcontraction of the muscles without simultaneously weakening them for useful voluntary movement". It has also been used successfully in Myasthenia gravis. Dr. PATON considers that the analysis of the action of this drug has cleared up some difficulties in our "knowledge of neuromuscular transmission and its response to drugs."

Hexamethonium and pentamethonium.—Both are ganglion-blocking salts and the former was first used in the treatment of raised blood pressure or hypertension. Modern observers believe that a certain nervous element plays a part in hypertension. Thus, activity in the higher centres of the brain (due for instance to worry) excited the autonomic nervous system with resultant rises in the blood pressure. A suitable compound which would block the ganglionic transmission and cause a fall in the blood-pressure, was therefore, found in Hexamethonium. The falls were found to be greatest in the upright posture and were really dramatic. Dr. PATON in his "Bengue Memorial Award" Lecture for 1952 delivered at the Royal Institute of Public Health and Hygiene on the 15th October 1952, detailed at length the prevailing view-points relating to the use of this drug in various other diseases besides hypertension. He considered that the lowering of the blood pressure with hexamethonium relieved the symptoms of hypertension. "It usually gets rid of the patients' headaches which are often disablingly severe, relieves breathlessness, improves or restores vision and improves his general sense of well-being. In eclampsia, too, it has sometimes enabled a live birth to take place, by arresting the progress of toxæmic hypertension". As regards recognisable pathological processes in hypertension, and alterations in the renal blood flow, PATON considers that some of the pathology can certainly be relieved, as for instance, an enlarged heart may get smaller in size, as the blood-pressure falls. In the retina, papilloedema will regress. Exudate will be absorbed and hæmorrhages may be cleared. If the kidneys have

been damaged already hexamethonium will not help. On the specific question as to whether it alters the renal blood flow, it is only possible to say that sometimes it is depressed, less often increased and sometimes unaffected. The action of hexamethonium in lowering the blood-pressure is accompanied by a widening of the blood vessels supplying the vital organs, like the heart and the brain.

The clinical and hæmodynamic effects of *intravenous* hexamethonium bromide in 30 hypertensive patients were found by WERKO *et al* to be much greater than those secured with sodium amytal or tetraethyl ammonium bromide (*Lancet*, 261, 470–72, 1951). The report of FULLERTON and MILNE on their experience with this drug in 31 patients in a Canadian Hospital, also points to the value and usefulness of this drug in the treatment of hypertension when given *intramuscularly*. They believe that the postural fall of blood-pressure was due to the use of hexamethonium (*Canad. Med. Assoc. Jour.*, Oct. 1951). BLAINEY made similar observations and obtained similar results on 34 patients with severe hypertension, (*Lancet*, 17-5-'52).

Dr. BRENDA MORRISON of Hammersmith Hospital, London, has now reviewed the literature on the use of Hexamethonium by 15 different workers who have given reports varying from "favourabe" to "doubtful" and furnished in a very interesting article (*Br. Med. Jour.*, 13-6-'53) his own experience on 39 hypertensive patients who received hexamethonium bromide *subcutaneously*; the patients were drawn from the complicated-essential, malignant and renal groups. He considers that the treatment routine and general management are of great importance in achieving successful results. Along with Dr. PATON, he also studied the clinical effects of a subcutaneous test dose of Hexamethonium in 16 normal subjects in relation to its concentration in the plasma. They found that for a given individual there was a close linear relationship between plasma concentration and the degree of blood-pressure reduction. No effects were observed which could not be attributed to ganglion-block, with the possible exception of 'drowsiness'.—(*B. M. J.*, 13-6-'53).

Amongst the defects noted, are :—(1) the gradually developing tolerance to the drug which necessitates increases in the dose so as to retain the therapeutic effect; (2) having to give the drug subcutaneously several times a day so that the patient has to live a sort of 'diabetic' *regime*; (3) balancing the dose under hospital supervision to start with; (4) the patient having to get accustomed to the symptoms of ganglionic block of other functions, (5) the impairment of renal-functions in some cases of malignant hypertension; and (6) the recent development recorded by MORRISON (June 1953) on the occurrence of dyspnœa and symmetrical opacities in the lung-fields on X-ray examination of 3 patients, after 15, 9 and 7 months' successful treatment respectively.

The advantages of treatment, however, particularly in the severe cases, are considerable, sometimes even life-saving. Substantial relief of symptoms and regressions of the signs in the eyes and in the heart are observed. The treatment is relatively safe, if due care is taken to adjust the dose carefully and the patient is warned about his sensitivity to posture. There have been very few toxic effects, and the drug is "cheap and easy to dispense". The combination of hexamethonium with other treatments is now being tried to avoid development of tolerance. Dr. PATON considers that hexamethonium might probably be tried in early cases of hypertension, so as to prevent renal and other complications developing later.

In France, hexamethonium bromide has been used successfully as a ganglion-blocking agent in cerebro-vascular accidents which result in hemiplegia, hæmatoma of the internal capsule of the brain and vascular thrombosis. Dr. PETIT DUTAILLIS *et al* consider that it might be effective in a hæmorrhagic infarct by helping to control the process and its encystment and also in arterial occlusion due to angiitis or embolism by relieving the capillary venous stasis and the perifocal œdema. (*Presse Medicale.*, 7-5-'52 and *J.A.M.A.*, 20-9-'52).

Hexamethonium has been used with success in cases of peptic ulcer in which both the acid secretion of the stomach and the motility of the stomach and intestines are suppressed: its action resembles that of atropine-like substances in this respect. More work will have to be done before the value of this therapy in peptic ulcer management can be finally assessed.

The third important use of hexamethonium says Dr. PATON, is to reduce bleeding at surgical operation, which was hitherto achieved at the level of the spinal cord, by means of spinal anæsthesia—a complicated procedure. Enderby (*Lancet*, 1 : 1145-1147 : 1950) employed for the same purpose a simple intravenous injection of a drug of transient action, whose effects can be readily antagonized. The three factors which contribute to the lowering of the pressure in the arterioles are stated to be the release of the vasoconstrictor tone causing a fall in blood-pressure., the use of a postural adjustment to pool blood in the dependent parts and the raising of the operation site above the rest of the body. The use of Enderby's technique is still in the experimental stage but the results of preliminary trials however, warrant further investigation.

Hexamethonium has also been used with success in spastic and various other types of peripheral vascular disease and in conditions where sweating of the hands is excessive. Where operation is not desired, hexamethonium therapy is simple and efficient. It has been found useful for depressing the overactivity of the small intestine which occurs in some forms of colitis or after gastrectomy. The

optimum dosage and conditions of safe usage however, remain to be investigated.

The abstract published at p. 413 of the ANTISEPTIC for June 1953 on the 'Newer Hypertensive Drugs' dealt with some aspects of the therapeutic use of hexamethonium. The action of this specific drug is based on the interruption of the autonomic activity by simple means.

The use of ganglion-blocking drugs such as hexamethonium in treating hypertension has stimulated the search for other drugs which will avoid the obvious difficulties and disadvantages of hexamethonium therapy. But the researches so far carried out on the pharmacology of the methonium compounds constitute one of the most valuable contributions to anæsthesia and therapeutics and illustrate in the words of Dr. PATON, the truth of the maxim "*it is never a waste of time to study in man the effects of a specific drug whose properties are properly analysed and understood.*" (The italics are ours).

Sodium Citrate in Vascular Disease

In 1945 Courbin, Chief Physician of the Hospitals at Bordeaux (France) administered intravenous injections of 1 gm. of sodium citrate in a 20 per cent solution to a 48-year-old hypertensive patient with vascular cerebral spasm with right hemiplegia, aphasia and coma. A fairly rapid regression of these occurred, following 12 such injections in 48 hours. Since 1946, Camelin and his associates of the Lyons hospitals, have used this method on 214 subjects, 50 of whom were out-patients. They stressed that there were no accidents in any of the cases, and that they never administer doses of more than 0·15 gm. per kg. of bodyweight. In order to prevent accidents owing to citrate anions, they perform a slow injection with a 10 per cent concentration. There was no effect of the citrate on the bleeding time and only a negligible influence on the coagulation time. As a precaution, they never applied this treatment when either of the two was prolonged.

This treatment is especially indicated for plethoric hypertensive patients with hypercholesterolæmia, azotæmia, frequent precordial pain, visual disorders and vertigo. All these symptoms subside within a week with sodium citrate, the maximum B.P., and the level of azotæmia fall by a few centimetres. Recent retinal changes improve. Ten seconds after the injection the patient experiences a peculiar feeling of freshness or a salty taste. Diabetic hypertensives also get relief. Cerebral vascular symptoms are rapidly influenced with one injection every third hour, according to Courbin's method (*supra*). Arteritis and diabetic arteritis are also amenable to this therapy. The experiments since made by Professors Binet, Vernes and others show that citrate may be effective against arterial atheroma provoked by vitamin D.—(*J.A.M.A.*, 150:2, 1952, p. 152).

MEDICINE AND THERAPEUTICS

Vitamin B_{12} in massive doses for herpetic lesions.—(Preliminary Report: Leitch, G. B., *Northwest Medicine*, April 1953).

Troublesome herpetic lesions, may prove to be much more tractable or even readily controlled, if response to the use of vitamin B_{12} in a small series of cases is found to be substantiated on more extensive use of this remedy.

The use of vitamin B_{12} in herpetic lesions, particularly herpes zoster is not new. Heyblon in May, 1951 reported treatment of eleven cases with recovery in eight in from 2 to 6 days. He recommended the use of only 30 micrograms daily for 8 days. The available literature contains however, no reference to the massive dosage employed in the series under report, which consisted of five cases, one of which was hospitalized due to the extensive and hæmorrhagic nature of the lesions and another was of herpes simplex. In all the cases pain subsided or ceased entirely within 24 hours of the initial administration of 1000 micrograms of vitamin B_{12}. Retrogression and healing of the herpetic lesions began in from 36 to 48 hours. Treatment was concluded in from 4 to 8 additional days, dosage gradually being reduced during the last few days. With one exception, peripheral neuritis was mild. The one case was controlled by mild sedation and the others were not treated. In none of the cases was there the least unfavourable reaction to the use of daily injections of 1000 micrograms intramuscularly.

The response in these five cases appears to be sufficiently encouraging and free from reactions that its further use either alone or in combination with other remedies such as thiamin chloride, is justified in these unpredictable and irregular conditions. Further investigation is necessary and should include studies of its influence if any, on the annoying peripheral neuritis which usually is a terminal feature and also the effectiveness related to the time it is administered in the course of the disease.

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Acute disseminated encephalomyelitis treated with ACTH.—(Miller, H. G., *Br. Med. Jour.*, 24, Jan. 1953, pp. 177—183).

The suggestion was made that cases of acute disseminated encephalomyelitis may have their foundations in an allergic vasculitis—'an urticaria of the nervous system'—and trial of cortisone or ACTH was also suggested.

In 1949, Pickar and Kramer (*S. Med. Jour.*, 42, 127) reported prompt improvement of a single case of encephalomyelitis, following antirabic vaccination, after the administration of diphenhydramine hydrochloride. Garrison (*Amer. J. Med.*, 12, 135, 1952) recorded "dramatic improvement" in a case of encephalomyelitis complicating antirabies vaccine (phenolized rabbit-brain virus) with large doses of cortisone (375 mg. daily for 2 days) and 100 mg. daily for the next 4 days). Great improvement was noted in 24 hours by which time his high fever had subsided. He remained drowsy for 4 days and anuria persisted for 6 days.

Miller of King's College, Newcastle-upon-tyre reports his results, in this paper, in a series of 7 cases of acute disseminated encephalomyelitis, treated with ACTH. Though the results cannot be considered conclusive, they suggest that the drug may have some value in the therapy of human encephalomyelitis in keeping with its known effectiveness in protecting animals against experimental 'allergic' encephalomyelitis.

All the seven cases clinically diagnosed as acute disseminated encephalomyelitis were deteriorating clinically at the time ACTH treatment was instituted. The first 3 cases were given ACTH by subcutaneous hyalase drip as a measure of economy but as increasing supplies of ACTH became available, six hourly intramuscular injections of 25 mg. were routinely given, augmented by occasional

additional injections, if a rise in the eosinophil count suggested that 100 mg. daily was physiologically ineffective. The seven cases comprise two of encephalitis following varicella, two of transverse and one of subacute ascending myelitis and 2 (familial) cases of encephalitic illness following non-specific infection, in one of which there have been recurrent encephalitic illnesses. Acute disseminated encephalitis has a tendency to rapid spontaneous and often complete recovery. It is believed however, that the results reported here are suggestive enough to justify further trial of ACTH in such conditions.

Butazolidin in arthritis.—(*Br. Med. Jour*, 27-12-1952).

Rhys Davies *et al* carried out a series of controlled tests in over 200 cases of rheumatoid arthritis and found that the improvement resulting from the use of Butazolidin was impressive, often dramatic.

Increased functional activity and considerable relief from pain were noticed in ankylosing spondylitis, painful Paget's disease of the bone and in degenerative joint disease. There was relief of pain in psoriatic arthritis, but no change in the skin lesion. It was very useful in rheumatic fever and the authors consider it as good as salicylate therapy.

The relief obtained usually lasts for about 3 to 7 days, rarely a few weeks. One gram daily in divided doses is given by mouth for 3 days initially, and then on alternate days for about two to four weeks. The dose is then slowly and gradually reduced to the lowest effective level, which has usually been found to be 600 to 800 mg. (in 3 or 4 divided doses) twice or thrice a week. As fluid retention is fairly common as a side-effect in Butazolidin therapy, it is better to avoid its use in older subjects and in those with impaired cardiac function and diminished cardiac reserve. Peptic ulcer patients also cannot be treated with this drug; but persons with chronic dyspepsia should be treated cautiously.

During treatment no alteration occurs in the E.S.R. or in Hb level, nor any improvement in muscle tone or bulk in those whose muscles showed wasting. Patients are advised to keep within limits in the matter of rehabilitation walking exercises, though as a result of the treatment they may feel relief from pain and be tempted to exceed their usual walking distances.

Beneficial effects of anti-coagulant therapy in congestive heart failure.—(*Ann. Int. Med*, pp. 865-886, Nov. 1952).

Thrombo-emboli were found in 210 out of 565 patients with rheumatic heart disease and congestive heart failure, autopsied at the Los Angeles County Hospital. In 114 patients, thrombo-emboli were the direct cause of death and in 28 patients did not contribute to death. Inspite of this fact, anti-coagulants have not been used widely as an adjuvant to routine therapy. In a study by Griffith *et al* of the Department of Cardiology of the University of South California Medical School, 629 patients with congestive heart failure have been carefully observed. A preliminary report on the first 300 patients was presented by Levinson and Griffith. Dicumarol, with Depo-heparin or Sodium heparin have been studied. The benefit of anti-coagulants through reduction of mortality and thrombo-emboli is, in this study twice that in the previous one. All patients with congestive heart failure who were admitted in the first year of this study into the medical wards of the Los Angeles Hospital, were serially allocated to control, dicumarol treated and Depo-heparin treated groups. During the second year of study, all patients with congestive heart failure admitted to the medical wards were treated in a conventional manner. On certain designated wards, the patients were used as controls, and did not receive anti-coagulants. The remaining wards were each assigned specific anti-coagulants, and patients admitted to these wards received anti-coagulant therapy according to a rigidly defined schedule. The anti-coagulants used were: (1) Dicumarol, (2) depo-heparin, (3) tromexan, (4) dicumarol *plus* depo-heparin and (5) dicumarol *plus* sodium heparin

The anti-coagulants were administered by the regular hospital staff. During both years, the patients were seen and examined frequently by the investigators (Griffith *et al*). Anti-coagulant therapy was continued till the patient was ready for discharge or free of congestive heart failure. Suitable tests were done systematically in every case prior to and during the administration of the anti-coagulants.

Results.—1. A significant reduction in fatality rate was observed in patients with rheumatic heart disease (over 40 years of age) and in coronary artery disease without hypertension. A significant reduction in thrombo-emboli was noted in heart disease of all ætiologies studied, except cor pulmonale and luetic heart disease.

2. Cardiac arrhythmia or a past history of congestive heart failure or thrombo-emboli did not influence the outcome in the treated or control series.

3. The various anti-coagulants studied appeared to be equally effective and beneficial. The advantage of rapid reversibility of hypoprothrombinæmia which was found with tromexan is a definite safety factor. It was found necessary to give the tromexan in a divided dose and to make twice daily determinations of the prothrombin level.

4. Hæmorrhagic phenomena were observed in 2·8 per cent of the control group and in 2·9 per cent of the treated series. Fear of hæmorrhage should not therefore, be a deterrent to judicious prophylactic anti-coagulant therapy.

5. A new and more efficient and satisfactory method for determining the prothrombin level was used. This was a modification of Owren's method and involves the dilution of the unknown plasma and the addition of an aliquot of prothrombin-free beef plasma. A stable, dried, easily reconstituted prothrombin standard is tested concomitantly with the unknown plasma and from the results obtained on serial dilution of the prothrombin standard an activity curve is constructed. The errors inherent in Quick's method apparently are eliminated in this method.

6. The concensus of opinion among the 30 resident physicians and the five investigators Drs. Griffith, Stragnell, Levinson, Moore and Ware, is that the addition of anti-coagulant therapy to the conventional treatment of congestive heart failure is distinctly beneficial but is to be undertaken only under strict clinical observation and an adequate, *dependable* anti-coagulant laboratory.

OBSTETRICS AND GYNÆCOLOGY

Tracheotomy in eclampsia.—(*Med. Newsletter*, Jan. 1953).

Tracheotomy has been found useful in poliomyelitis, tetanus, and in numerous other conditions in which respiratory depression due to obstruction of the tracheobronchial tree by secretions, requires prolonged endotracheal aspiration. Collins and his coworkers *at the* Tulane University, New Orleans treated 86 patients with convulsive toxæmia between 1946 and 1951. Only patients with convulsions are considered here and none of those with severe eclampsia, with coma and all the other signs but not convulsions. None without convulsion died. Tracheotomy was performed in addition to the routine customary measures, in 8 patients with convulsive toxæmia and in two with non-convulsive toxæmia. Of 7 who died, two had the benefit of tracheotomy. In one of these, a second and fatal cerebrovascular accident occurred 13 days subsequent to removal of the tracheotomy tube and apparent recovery. In the other tracheotomy was done too late to be of use. Many of the 8 patients who had tracheotomy, would have died, if it had not been performed. Of the 5 who died prior to this utilization of the surgical procedure, four showed marked respiratory distress and died within 24 hours of admission; the other died 4 days after admission, with respiratory failure as the marked symptom.

The authors do not advocate tracheotomy in every case of eclampsia but they certainly recommend it in cases

where airways and suction fail to maintain adequate ventilation of the lungs or where laryngospasm develops: Tracheotomy sets should be an essential item in the equipment of all delivery sets. No ill-effects from tracheotomy have been observed.—(*Am. J. Obst. Gynaecol.*, 63 : 5, 1952).

A simple method of preventing fœtal anoxia.—(Dunlap, J. C., *Am. Pract.*, 3 : 214-217, March 1952 and *Qr. Rev. Surg. Obst. Gynaec.*, Dec. '52).

Anoxia has repeatedly been indicated as the basic cause of fœtal cerebral damage and death. It has been shown that regional nerve blocks interfere less than inhalation anæsthesias with fœtal oxygen tension; however the technical difficulties involved in the administration of caudal and spinal anæsthesias make these procedures impractical for wide use away from adequately staffed hospitals. To prevent fœtal anoxia, a simple technique for saturating the mother and fœtus with oxygen, along with an equally simple method of analgesia and anæsthesia, is presented in this article by Dr. Dunlap.

One hundred per cent oxygen is administered during the last ten to twenty minutes of the first stage of labour and during delivery by means of a B.L.B. mask at a flow rate of 7 litres per minute. Analgesia is achieved during the first stage of labour by one hypodermic injection of 100 mg. demerol and 1/150 gr. of scopolamine. Anæsthesia is produced by performing pudendal block, and during actual delivery this anæsthesia is augmented by slowly injecting 100 mg. demerol intravenously.

At the Los Alamos Medical Centre (altitude 7337 feet) 108 women were delivered by this method. Six of them had toxæmias of pregnancy. Of the 108 infants delivered, 106 were in excellent condition, as judged by the prompt breathing and lusty cry, pink colour and good muscular responses. Cord and placental anomalies probably accounted for distress in 4 of these fœtuses prior to birth. There were two antepartum fœtal deaths.

The benefits of oxygen saturation for both mother and child are really great and the technique is therefore, strongly advocated as deserving of more extensive trials and clinical investigation.

Lesions of the vulva.—(Hunter, W., *Med. Prac.*, 224, 613).

When dealing with lesions of the vulva, disease of the pelvic organs and disease of the skin must be excluded. Kraurosis vulvæ is considered to be a retrogressive condition affecting the vestibule and vaginal orifice of an atrophic vulva, and occurring typically in post-menopausal patients. It is not pre-cancerous and is helped by œstrogens, stilbœstrol 2 to 3 mg. daily or dienoestral 0·3 mg. thrice a day.

Leukoplakia vulvæ is considered as being pre-cancerous and primarily affects the labia majora and prepuce of the clitoris. In the early stages there is hyperæmia of the skin and later the skin become coarse, and dull-white in colour. There may be thickening of the epithelium and the papillæ may be hypertrophied. Later it shrinks, fissures appear and sooner or later epitheliomata may develop. Hypochlorhydria and vitamin A deficiency are usually present in this condition. Bowen's disease of the skin and mucous membranes, epithelioma and simple chronic vulvitis, gonorrhœa, syphilis and chancroid, and other lesions that may affect the vulva have also been mentioned along with the signs and symptoms characteristic of them.

The ureters in complete procidentia.—(Backer, D. C., *J. Obst. Gynaecol. Br. Emp.*, 59 : 382-384, June 1952).

Though all are agreed on the fact that the ureters are displaced or distorted in some cases of procidentia, the literature on the subject is however, scanty and vague. If the displacements of the ureters is sufficient to give rise to obstruction, it is manifestly a point of great importance. Backer studied 24 cases by means of ascending and descending pyelography and blood urea

determinations. Most of the 24 patients were elderly, six being over 75 years of age.

Some urinary tract obstruction was revealed in 30% of cases but only two of the twenty four women showed a blood urea level of over 50 mg. per cent. Backer records that in his experience these elderly ladies tolerate surgery extremely well and he discusses the type of case suitable for a Manchester repair or for a Le Fort operation.

Vaginal hysterectomy is contra-indicated in the elderly patient.—(*Author's Abstract*).

The menstrual cycle: A recent advance in oestrogen therapy.—(*Am. Jour Obst. Gynaecol.*, 64: July 1952 and *Q. Rev. Surg. Obst. and Gynaec.*, 9: 4, 1953).

The clinical effectiveness of piperazine œstrone sulphate (Abbott's Sulestrex) was first determined on the basis of subjective relief, and also on vaginal bio-assays in 25 women with menopausal symptoms. An additional 100 patients similarly treated responded satisfactorily in 9 of 10 cases. Of 20 patients with severe symptoms only 2 of 3 got relief. The lack of response in at least a third of this group was attributed to other ætiological factors (psychogenic ?) and not to a failure of medication but rather to an incompatibility of diagnosis and treatment.

50 parturient women were tested with this drug for inhibition of lactation. The time of administering the therapy was found to be the factor influencing lactation; thus, when started within the first 24 hours after delivery 90 per cent obtained optimum results. Therapy was successful in less than 50 per cent of the patients, when lactation had been established.

Twentyfive patients in menopause received a combination of piperazine-œstrone-sulphate and testosterone but there was no difference in the results obtained.

Piperazine-œstrone-sulphate is the purified chemical form of natural œstrone sulphate combined with piperazine (di-ethylene-diamine) to form a stable salt. The buffer action thus imparted ensures stability of unvarying physiological activity and banishes the urinary odour and taste often associated with the natural female hormones obtained from the mare's urine

No symptoms of intolerance was noted throughout this study. Withdrawal bleeding occurred in 4 of 200 cases but was of such a nature that cessation of therapy was required in only 2 patients. The preparation appears to promote quick clinical response with an unusual minimum of side reactions. Reich and his coworkers of Chicago advocate the use of this preparation in all cases where œstrogen is indicated.

DERMATOLOGY

Procaine hydrochloride given intravenously in pruritus.—(*Arch. of Dermat. and Syphilol.*, 65, 39–44, 1952). Beinhauer and his co-workers gave procaine hydrochloride intravenously to 181 patients with pruritus. The majority had been treated with other methods without benefit. A dose of 500 c.c. of a 0·1 per cent to 0·2 per cent solution of procaine hydrochloride in normal saline was best tolerated when given over a period of 60 to 90 minutes. Barbiturate was given one hour before injection and 200 mg. ascorbic acid was added to each infusion to increase the resistance against toxic side-effects and also to assist patients who were undernourished. When œdema was present 5 per cent glucose was added. In patients with nervous irritability and fear of the infusion, thiopental sodium in doses of 200 to 300 mg. added to the first two or three injections relieved the pruritus and allowed the patient to sleep. This modified treatment proved particularly effective in generalised neuro-dermatitis. Most patients received one injection every day and it was found that if the pruritus was not relieved in six such injections, further therapy with this drug was useless. The majority of patients obtained relief with 4 injections. Complete relief was secured in

59 patients and temporary relief in 67. Fiftyfive got no relief. The treatment is safe when properly controlled, and can be tried when other measures fail. Contraindications for this therapy are :— allergy to procaine, myasthenia gravis, thyrotoxicosis, and treatment with digitalis or digitalis-like drugs.

Zinc peroxide in treatment of surgical infections.—(*J. Am. Med. Assoc.*, 1952, 149, p. 1449).

Meleney is of the opinion that sulpha drugs and antibiotics have not entirely supplanted zinc peroxide in the treatment of surgical infections. Zinc peroxide is most useful especially in undermining burrowing ulcers, in synergistic gangrene after excision and in decubitus ulcers, in diabetic gangrene, also in evil-smelling and foul lesions of the mouth and neck and in radiation burns, besides many other conditions. It is most active and effective in a watery suspension but can be used in a carbowax base.

Methobarbital successful in hyperhidrosis.—(*J. Am. Med. Assoc.*, 150, 28 : 1952 ; *Br. J. Dermat.*, Apr. 1953).

Dr. Scanlon treated two cases of severe hyperhidrosis with 0·2 and 0·4 gm. of methobarbital daily. It is believed to act on the diencephalon. In effective doses it produces less narcosis in anxiety states than other barbiturates and does *not* produce the mydriasis, the dry mouth and the constipation met with frequently when Banthine is administered. Scanlon recommends this drug in preference to others, particularly for hyperhidrosis of emotional origin.

The use of neomycin in dermatology.—(*Jour. Amer. Med. Assoc.*, 148 : 339-343, 1952).

Kile and his coworkers report the results of treating 869 patients with skin diseases of various kinds. They used Neomycin (derived from *streptomyces frudiae*) as an ointment in the strength of 5 mg. per gm. in two bases, one water-miscible and the other oily. The latter was effective in infective dermatoses. Wet compresses containing 1 mg. per cc. were found to be quite effective too. Pyogenic dermatoses improved in two to five days. Only one patient out of the 869 developed sensitivity to neomycin and in 9 cases there was some irritation. Some patients with infections due to hæmolytic streptococci or *pseudomonas aeruginosa*, did not respond quite so satisfactorily to neomycin. By and large, this new antibiotic gave better results than any other topical application.—(*Abst. W. M.*, 12 : 2, 1952).

Plantar warts treated successfully with podophyllin.—(*Arch. Derm. Syphil.*, 65, p. 490, April 1952).

Dr. Walz treated 13 patients with plantar warts using podophyllin resin in Tinct. Benzoin and obtained cures in eleven of them without recurrence in 4 to 6 months. The wart was pared down until the red capillary ends became visible ; then a 25 per cent solution of podophyllin in Tinct. Benzoin was applied to the area. Allowing 20 to 30 minutes for the solution to dry on the surface, a vaseline dressing was applied ; this was removed everyday before bathing. The treatment was repeated at intervals of 5 to 7 days. A definite improvement was noticed even after two applications accompained by relief from pain and a reduction in the keratin-piling. After eight to ten such treatments the area was usually clean of any trace of the wart. In the apparently cured patients, normal epidermis appeared over the wart area. A large wart in one of the patients, which measured 1·25 inches in diameter and about ¼ inch in depth required only 8 treatments to disappear and did not recur in 6 months.

Riboflavin in the treatment of psoriasis.—(*Jour. Investig. Derm.*, April 1952, 305-306).

Dr. Maynard treated over 200 cases of psoriasis with riboflavin, 5 to 10 mg. once a week intramuscularly and daily doses orally. No local applications were made until the patient responded to riboflavin, and then only the few resistant lesions were treated by local applications to hasten the cure and to produce cosmetic effect. 148 of the 200 and odd cases were followed-up by

Dr. Maynard ; 37 cases had completely healed up ; 77 showed marked improvement ; 24 had improved 50 per cent or more ; 4 showed less than 50 per cent improvement and only 6 failed to respond. No cases became worse.

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B. C. G. and leprosy.—Reviewing the available information on Leprosy, Dr. Nelson Souza Campos of Brazil, first discussed its pathogenesis which is not fully understood because of the impossibility of culturing or animal inoculation of the bacillus. He divided the clinical types of the disease into "*chronic benign*" and "*acute serious*" cases. The lesions are essentially polymorphous and the evolution of the clinical forms variable. The lepræ bacilli do not occur as different strains. Thus, the clinical evolution must depend on the body's predisposition or its powers of resistance.

Contact alone is not sufficient to cause the disease, there *must be* a certain pre-disposition in the individual if the infection is to occur. Prophylaxis in leprosy is, in the author's opinion, based on immunological principles. The immune allergic state in leprosy is measured by the '*lepromin test*'. Observations and experimentation have clearly shown that lepromin positive persons are resistant to infection and those who are lepromin negative are susceptible. The high percentage of positive tests among healthy persons in countries where leprosy is endemic or even absent makes one think that a positive test is *not* solely the consequence of a specific reaction of the body to a previous leprosy bacillus infection. Other factors must be involved in this phenomenon. Dr. Campos pointed out the high prognostic value of the lepromin test, which, when positive, reveals the benign cases, easily curable or curable spontaneously, and when negative, reveals the malignant forms.

Dr. Nelson Souza Campos next mentioned his experience with BCG vaccine given to a group of young children who subsequently had a positive Mitsuda (lepromin) test. In the concluding portion of his report he called attention to the need for similar studies in other centres taking different samples of the population and observing the results over a longer period. Mass lepromin testing would also be useful among those immunized by BCG vaccine particularly in places where this method has been used for many years.

From the generalized adoption of BCG vaccination in a known area of leprosy prevalence, in time, one could get data that might justify compulsory vaccination.—(Foreign letter, *J. A.M.A.*, 12-4-1952).

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Modern treatment of leprosy in a nut-shell.—It evolves around general hygienic measures, adequate diet including the administration of vitamins, calcium and iron and the elimination of intercurrent infections. Specific measures consist of the administration of various sulphones such as sulphetrone in the form of a 50 per cent aqueous solution and a 25 per cent emulsion for parenteral administration. The dosage is usually 5 to 10 cc. twice a week for several years. Diasone is another effective sulphone and is given orally as 0·10 gm. tablets thrice a day for three weeks, then no medication for the fourth week, followed by a repetition of the schedule. The average total dose over an 18 month period is 320 gm. Promacetin, a new sulphone offers even greater therapeutic promise, as does thiacetazone. The latter drug has two marked advantages over the sulphones in that it does not cause mental depression nor is there any evidence that it causes anæmia or lepra fever.—(H. T. Behrman in *Scalp in Health and Disease*, '52, p. 272).

OPHTHALMOLOGY

When to operate for cataract.—(Rones, B., *Sight Saving Review*, Spring, 1953).

Until about 20 years ago, the answer was fairly simple, for it was "when the cataract is ripe". This waiting for maturity of the cataract entailed a delay and incapacity of many years, during which the patient was not able to earn his livelihood or to carry on a

normal life. There was a definite reason for such procedure in those earlier years, however, for with the extra capsular type of surgery which was safest at that time, the maturity of the lens was the best indicator of the ease with which the cortex could be completely removed. It had been found that most of the complications and bad visual results following an operation were caused by the retained cortex. During the last two decades however, the intra-capsular cataract operation together with the use of corneoscleral sutures has radically altered the indications for surgery. In this type of operation it is no longer necessary to use the maturity of the cataract as the criterion, for a lens with a slight opacity can be returned just as easily as one with a mature cataract. In consequence a new set of criteria has been developed.

Intra-capsular operation:—The difference between the extra-capsular and intra-capsular operation for cataract can best be exemplified by using the analogy of a grape. In the extra-cellular type of operation the skin of the grape would be cut and the contents expressed by pressure leaving the fragments of the grape adherent to the skin which would remain *in situ*. In the intra-capsular type, the skin of the grape would be grasped and by a combination of traction and pressure, the entire grape would be removed skin and contents intact. This latter procedure offers by far the most favourable results and should always be the procedure of choice. It however, requires a considerably greater degree of dexterity and skill on the part of the surgeon and the chances of failures are for the occasional operator far greater than with the older method. Complications have been minimized and visual results greatly improved by the suturing of the operative wound, by the use of retrobulbar novocain injections, by sodium pentothal anæsthesia and by removal of the lens through a round pupil; with the present day technique of the cataract operation we will be safe in promising the patient a 95 to 98 per cent favourable chance of the restoration of good vision. By the modern method of intra-capsular round-pupil surgery with the use of corneoscleral sutures, patients are now allowed to have the unoperated eye exposed on the day following the operation or even on the day of operation. They are allowed to sit up, out of bed the day after the operation and permitted to walk round the room a day or two later. Everything is done to keep them relaxed and cheerful and not to make introspective, nervous individuals of them.

Terramycin in trachoma.—(*Eye Clinic*, Istanbul., and *S. S. Rev.*, p. 46, Spring 1953).

Dr. Izzet Bilger reports the results of treatment of 700 cases of trachoma in the Adana Trachoma Hospital at Istanbul. Terramycin hydrochloride was administered *per os*, 250 mg. in capsules, 0·1 per cent and 0·5 per cent ointment and 0·5 per cent solution of eyewash. Of 38 patients with acute trachoma 27 recovered after 3 to 6 weeks and 11 after 5 to 10 days. 27 patients who were given terramycin orally, ointment and eyewash, recovered after 20 days, but a slight gastrointestinal irritation developed.

Patients with chronic trachoma required from two to three months of intensive therapy for complete recovery and in order to prevent a relapse the treatment was usually continued for a further 4 weeks. A combination of chemotherapy and surgical intervention in chronic and complicated cases accelerated recovery.

From a special school for children with trachoma, 640 children who had chronic trachoma were selected and divided into 3 groups. The patients in group one received only terramycin; the second group had terramycin and chemotherapy and group 3 received terramycin, chemotherapy and surgical treatment. In almost all patients bleeding and suppuration decreased in from one to two weeks, and after two to six weeks 20 per cent of the patients recovered. Eighty per cent recovered after 12 weeks, but the therapy was continued for a month after recovery to prevent relapses.

REVIEWS OF BOOKS AND PERIODICALS

Side Effects of Drugs—By L. MEYLER, Consulting Physician at Groningen (Netherlands). Translated by PH. VINJSJE and W. MULHALL CORBET, Amsterdam, 1952. Published by Elsevier Publishing Company, Amsterdam, Houston, London, New York. Printed in the Netherlands by N. V. Drukkerij G. J. Thieme, Nijmegen.

A concise book written with the sole purpose of deprecating the indiscriminate use of drugs likely to bring about harmful effects by such indiscriminate use. In this book the author deals only with the various harmful side effects of drugs, which can result either by over dosage, or prolonged use or individual hypersensitivity. The material is gathered from published literature and from several medical journals, all of which have been listed at the end of each chapter. As one reads the book, one is appalled at the number of major and minor side-effects, a drug can cause, all of which have been beautifully and concisely summed up in this book.

Besides the preface by the author, there are about 25 chapters and each chapter deals with the side-effects of a particular category of drugs. In this way, the side effects of almost all the known varieties of drugs, including blood, blood derivatives and plasma substitutes and sera and vaccines have been covered in this small book of 268 pages, which is also well indexed.

This book will serve as a real eye-opener to many practising physicians who make injudicious and indiscriminate use of some, if not all of the drugs. It is a book that ought to be read by every practising physician, desiring to have a better knowledge of the drugs which he handles. U. C. B. B.

Studies in Pædiatrics–By Dr. A V. S. SARMA, M.B., B.S., D.C.H. (Lond.), F.D.S. (Lond.), Madras.

Dr. T. S. Tirumurthi has aptly remarked in his foreword that the "book on Studies in Pædiatrics is not meant to serve as a text book for students but contains the author's personal observations and experiences in some of the diseases of children both common and rare which were specially studied by him." The author Dr. A.V.S. Sarma, needs no introduction to the readers of the ANTISEPTIC. He has been in the field of Pædiatrics for quite a number of years and has been regularly publishing the fruit of his labours and experience, from time to time in the ANTISEPTIC and other medical journals. Rightly feeling that there is something of abiding and permanent interest and value in these articles the author has now brought them out as a separate booklet.

Several ailments have come under the observation of Dr. Sarma,—ailments common as well as rare. Common diseases like cyclic diarrhœa of infants, infantile convulsions, infantile hepatic cirrhosis, cœliac disease, tuberculous meningitis and whooping cough have been dealt with in the respective essays with such great care and precision that the general medical practitioner may well feel that his knowledge of the treatment of these diseases has been greatly augmented. The author's notes on the rarer diseases like Schilder's disease, Gargoylism, Simmonds' disease, Renal Rickets etc. may prove helpful to practitioners in the early diagnosis of such diseases.

Of particular interest is the essay on "A Panoramic View of Pædiatric Practice" where the author is able to arrive at certain conclusions regarding the incidence of diseases among children based on statistics collected by him from cases admitted in the Government Royapettah Hospital and from his examination in 1949 of the children of a big school.

One would wish the author had included common tropical diseases of children in his studies. This is a field not exhaustively covered so far. Notes on such diseases by specialists like Dr. Sarma would be useful additions to the limited knowledge we have on the subject at present.

That Dr. A. V. S. Sarma is a keen student of pædiatrics is evident from

his observations which are published in this booklet which also contains many clinical photographs that are self-explanatory. The printing and get-up of the book are of a high standard.

"Studies in Paediatrics" is a good reference book and will be useful to every general practitioner who is after all a paediatrician in a small way.

U. S. R.

Special Number : "The Indian Medical Journal", 538, Narayan Peth, Poona-2. Price Rs. 2/-

We have received the special number on '*Medical Education*' of the *Indian Medical Journal* for June 1953, which has been brought out in the context of the International Conference on Medical Education due to meet in London this month, at which India will doubtless be represented. The Union Minister of Health, Rajkumari Amrit Kaur reiterates her view on the need for an uniform standard for basic medical training and the maintenance of high standards for post-graduate medical education.

Dr. Clegg, the Editor of the *British Medical Journal*, has raised a pertinent point when he says "If the aim of the medical education is to produce a practising doctor who can be let loose on the public, then we should ask whether the curriculum is designed to meet this end.....If the teaching of the medical student falls more and more in the hands of the specialists, then slant will be towards turning out specialists and not '*general doctors*'. As most doctors become general practitioners, are they encouraged to become so, during their training and is the curriculum directed to this end? Are the qualifying examinations directed to this end? Does the medical student really need to learn the relationship of the posterior triangle of the neck or the details of the radium treatment of the carcinoma of the cervix uteri?"

The conception of a '*Basic doctor*' fits in with the modern trends in medicine, requiring a thorough and immediate reorientation. There has been felt in many countries of the world, this urgent need for reorientation of medical education and the proposed London Conference is certainly the outcome of the intensity of the general feeling amongst medical educationists and the discerning public.

A number of very thoughtful and interesting articles from well known leading medical men connected with medical education in India, have been published in this issue.

The Editors have been thoughtful in reproducing relevant reports and opinions of leaders of thought, and of Education Commissions *e g.* Radhakrishnan Commission and Bhore Committee. They have also reproduced three very valuable articles which appeared in the Bulletin of the World Medical Association in Oct. 1952, in order to enable the readers to understand and visualize the purpose and aims of the International Conference on Medical Education to meet in London in August 1953.

T. N. S. R.

BOOKS RECEIVED

The following books have been received with thanks since 15-7-'53 and the courtesy of the Publishers in sending them is acknowledged. Reviews will appear in due course.—ED.

1. **Hints on the Assessment of Sub-Standard Risks in Life Assurance**—By Dr. B. B. DOTTO, 1953, Medico-Insurance Publications, Calcutta. Price Rs. 2/-
2. **The Medical Annual 1953**—Edited By Sir HENRY TIDY, K.B.E. M.A., M.D., (OXON) F.R.C.P., and Dr. A. RENDLE SHORT, M.D., B.S., B.SC., F.R.C.S., 1953. M/s. John Wright & Sons Ltd., Bristol. 8. Price 27s. 6d.
3. **Kshayaroga Mathu Adara Nivarane**—By Dr. V. R. BHAT, M.B., B.S., T.D.D. (M.), The Chitra Prakashna Mandira, Mangalore-3. Price Rs. 2/4/-

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CORRESPONDENCE

I

The Shortened M.B.B.S. Course—Discontinuance by the Madras University

To the Editor, ANTISEPTIC, Madras.

Dear Sir,

The news that the above course is to be discontinued from April 1953 onwards by the University of Madras, though very disappointing has come at an inopportune moment unawares to the profession at large and the bulk of Medical Licentiates in particular. The reasons underlying the abolition of such a useful measure which gives facilities to aspiring Medical Licentiates to obtain the M.B.B.S. degree can neither be appreciated nor understood at the present juncture when the purpose for which this course was intended is not served, apart from the cherished objects of the profession to bring about a uniform standard of medical education in our country.

The establishment of a uniform standard of Medical Education and the Unification of the Civil Medical Services in this State was a result of the persistent efforts of the All-India Medical Licentiates' Association. When the L.M.P. Course was abolished, this Association with its leaders and elders in the profession brought into existence the Condensed M.B.B.S. Course for Medical Licentiates aspiring to take the M.B.B.S. Degree. Since then that course has functioned without let or hindrance. As ill-luck would have it, the choice of candidates for admission has been restricted. Those with War Service, in Government Service, District Boards and Local Funds and a few private medical practitioners with similar qualifications were chosen. The regulations governing admissions were relaxed for the admission of candidates from other States. Thus many of the latter category were chosen to the detriment of those in our State. Year after year our own candidates have failed in their attempts to gain admission. I know of a candidate of our State applying for a seat continuously for seven years, the last attempt being in the month of July 1952, in vain. There are a few others with lesser expeditions but got disappointed all the same. Such frustration of the efforts of candidates made me approach the Minister of Health and the Vice-Chancellor of the University of Madras and draw their attention to the nature of the choice etc. and the desirability of giving fuller opportunities for those eager to avail themselves of the Condensed Course. I believe, that there are candidates waiting to be chosen from our State, apart from those on the waiting list.

The main objective of the profession is to bring about one standard of medical education and qualification in India, affording opportunities to the numerous licentiates who wish to avail themselves of the facilities for higher medical education to do so, and thus obtain recognition in their own country. The Medical Schools existing in a few States should be made Colleges by the efforts of the State Governments The Indian Medical Council also should take steps in this regard: it should not recognise the Diplomas of such schools in cases they continue to exist. Meanwhile, we should endeavour to afford chances for all those medical licentiates aspiring for higher qualifications to acquire them in their own country.

In the profession of medicine there is no caste, creed or colour, just as disease and suffering know no caste or creed and undue restrictions and limitations mar its scientific progress. It would be a sorry state of affairs if, in the Indian Republic where every citizen enjoys equal privileges and rights, there should exist any bias or barrier against their legitimate ambitions. A provincial or parochial out-look would hamper the growth of sound medical education of the medical licentiates in our country and it is against the tradition of the University of Madras which serves as a model to other States in the Indian Union in the wake of medical reforms and achievements to its credit. I fervently hope the University of Madras would change its attitude and extend this desirable concession up to the year 1956, as resolved by the Indian

Medical Council at its last meeting. This would enable those on the waiting list to continue their studies for the M.B.B.S. degree.

Madras-17. 18-5-1953. D. V. VENKAPPA, *Regd. Medical Practitioner.*

* * *

II

The Shortened M.B. B.S. Course

To the Editor, ANTISEPTIC, MADRAS.

Dear Sir,

The deputation which met the Minister of Public Health at the Secretariat on the 13th July 1953 has done a great service to a section of medical men aspiring for higher medical educational facilities in the Madras State. It is indeed very kind and generous on the part of the Health Minister to have evinced a keen interest in the continuance of this course—a necessary item for the maintenance of a uniform standard of medical education. In spite of all the endeavours of medical licentiates to obtain the University Degree, it is a matter for deep regret and concern that the Board of Studies of the University should not have given their serious thought before the closure of this useful measure. It is equally surprising and painful to note that no notification or publicity was ever given in this regard to let the public and the profession know about this unfortunate decision. The State of Madras had gone ahead of the other States in the Indian Union in matters of medical education and medical reforms and as such it is imperative on the part of the University to continue this desirable reform as long as it may be necessary. A sudden closure is sure to have its deleterious effects on the profession. It is heartening that the Indian Medical Council atleast had thought it fit and extended the term of the course up to the year 1956. It is necessary and desirable that the Madras University should fall in line with the suggestion made by that Council. It behoves therefore, the University to continue this desirable course atleast from next year onwards till such time as the medical licentiates resident in this State desirous of fulfilling their cherished ambitions to obtain the Degree in Medicine in their own country have done so. I take the opportunity of conveying to the Minister our heart felt thanks for his generous gesture, to the deputation for having done its duty and to the Press for espousing this just and desirable cause by giving it the requisite publicity.

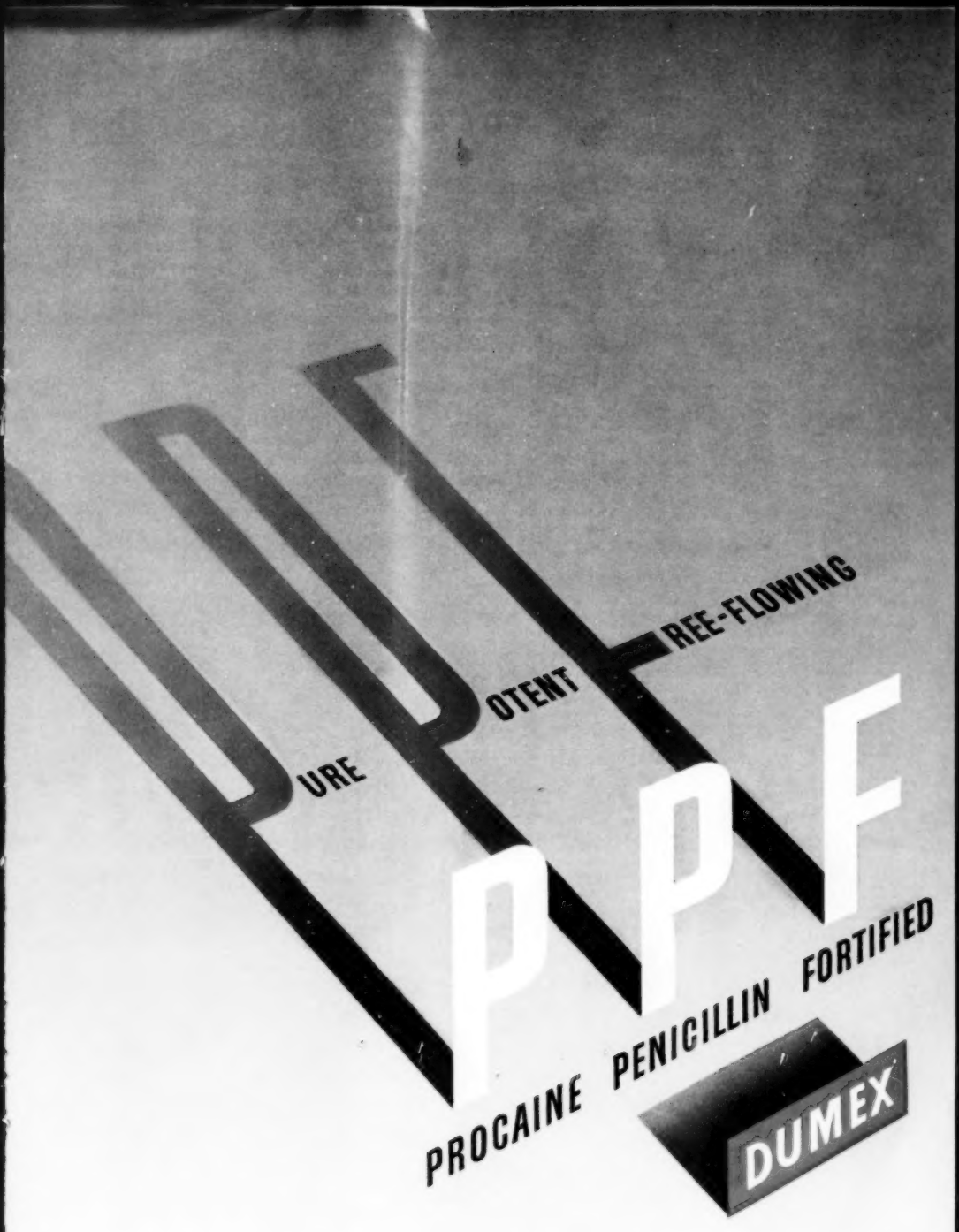
It was opportune that the deputation raised the question about fees being levied for meetings of the Madras Branch of the Indian Medical Association by the Authorities of the Medical College whilst no such fees or restrictions were enforced hitherto. The Minister viewed the matter sympathetically and stated that he would write to the College Authorities. Another subject of great importance was brought to his notice about the site for a building for the Madras Branch of the Association and a particular central area in the gift of the Government was then pointed out as very suitable. The Minister felt the request reasonable and desirable and stated that he would move in this matter also. The Members who took an active part in these deliberations were Drs. K. C. Nambiar and P. Natesan, President of the South Indian Provincial Branch and the Madras City Branch respectively, whilst the other Members of the Deputation who participated by their willing cooperation were Drs. T. S. Tirumurti, D. V. Venkappa, A. V. Avadhani and N. B. Shetty.

Such of those medical licentiates as are really keen and desirous of undertaking the Condensed M.B. B.S. Course may apply to the undersigned for further details in order to enable him to finalise the list of such of them as are resident in the Madras State.

"Dayalbagh" No. 3, Dinadayalu Street, T. Nagar, Madras-17. 23rd July '53. D. V. VENKAPPA, L.M.P., *Regd. Medical Practitioner.*

CORRIGENDUM

Page 436, ANTISEPTIC, Vol. 50 : 6, June 1953. The word '*glaucoma*' in line 11 of para 2 in the above page is a misprint for '*leucoma*'. The error is regretted. (Ed. ANTISEPTIC).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